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NEWS 2 MAY 01 New CAS web site launched
NEWS 3 MAY 08 CA/CAplus Indian patent publication number format defined
NEWS 4 MAY 14
                RDISCLOSURE on STN Easy enhanced with new search and display
                fields
NEWS 5 MAY 21
                BIOSIS reloaded and enhanced with archival data
NEWS 6 MAY 21
                TOXCENTER enhanced with BIOSIS reload
NEWS 7 MAY 21 CA/Caplus enhanced with additional kind codes for German
                patents
NEWS 8 MAY 22 CA/Caplus enhanced with IPC reclassification in Japanese
                patents
        JUN 27
                CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 9
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NEWS 12 JUL 02 LEMBASE coverage updated
NEWS 13 JUL 02 LMEDLINE coverage updated
                SCISEARCH enhanced with complete author names
NEWS 14 JUL 02
NEWS 15 JUL 02
                CHEMCATS accession numbers revised
NEWS 16 JUL 02 CA/CAplus enhanced with utility model patents from China
NEWS 17 JUL 16 CAplus enhanced with French and German abstracts
NEWS 18 JUL 18 CA/CAplus patent coverage enhanced
NEWS 19 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 20 JUL 30 USGENE now available on STN
NEWS 21 AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 22 AUG 06 BEILSTEIN updated with new compounds
NEWS 23 AUG 06 FSTA enhanced with new thesaurus edition
                CA/CAplus enhanced with additional kind codes for granted
NEWS 24 AUG 13
                patents
NEWS 25 AUG 20 CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
             CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
             AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.
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=> file reg

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## => e raloxifene/cn RALOX LC/CN E1 1 E2 RALOX-A/CN 1 E3-1 --> RALOXIFENE/CN E4 RALOXIFENE HYDROCHLORIDE/CN 1 E5 1 RALOZAM/CN E6 3 RALSTONITE/CN RALSTONITE (ALF2 (OH))/CN E7 1 RALSTONITE (ALF2(OH).1/2H2O)/CN E8 1 E9 1 RALTAT 10/CN RALTEGRAVIR POTASSIUM/CN E10 1 E11 1 RALTITREXED/CN E12 RALUBEN/CN

=> s e3

L1 1 RALOXIFENE/CN

=> d l1 1 ide

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN

RN 84449-90-1 REGISTRY

ED Entered STN: 16 Nov 1984

CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl] [4-[2-(1-piperidinyl)ethoxy]phenyl] - (CA INDEX NAME)

OTHER NAMES:

CN Keoxifene

CN LY 139481

CN Raloxifene

CN [2-(4-Hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-(2-(1-piperidinyl)ethoxy)phenyl]methanone

MF C28 H27 N O4 S

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB\*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC, PHAR, PROMT, PROUSDDR, RTECS\*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL (\*File contains numerically searchable property data)

Other Sources: WHO

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1751 REFERENCES IN FILE CA (1907 TO DATE)
38 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1763 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 8.25 8.46

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 13:29:27 ON 21 AUG 2007
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FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9 FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.

They are available for your review at:

## http://www.cas.org/infopolicy.html => s l1 1763 L1 T<sub>1</sub>2 => d scan L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN CC 1-0 (Pharmacology) TI Osteoporosis treatment and limitations and perspectives review bisphosphonate raloxifene parathyroid hormone fall prevention disuse syndrome Bone, disease IT (fracture; osteoporosis treatment and limitations and perspectives) IT Anabolic agents Osteoporosis (osteoporosis treatment and limitations and perspectives) Diphosphonates IT RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (osteoporosis treatment and limitations and perspectives) 13598-36-2D, Phosphonic acid, alkylidenebis-derivs. IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (Bisphosphonate; osteoporosis treatment and limitations and perspectives) 9002-64-6, Parathyroid hormone ΙT RL: BSU (Biological study, unclassified); BIOL (Biological study) (osteoporosis treatment and limitations and perspectives) **84449-90-1**, Raloxifene 129318-43-0 TT RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (osteoporosis treatment and limitations and perspectives) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN CC 1-1 (Pharmacology) TI Validation of a novel HPLC method for the determination of Raloxifene and its pharmacokinetics in rat plasma ST Raloxifene detn plasma HPLC; liq chromatog Raloxifene plasma; pharmacokinetics Raloxifene plasma Blood plasma IT Pharmacokinetics (pharmacokinetics of Raloxifene in blood plasma of rats after oral dose) IT Blood analysis HPLC (validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma) IT 84449-90-1, Raloxifene RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study) (validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN

CC 1-8 (Pharmacology)

TI Effect of genistein and raloxifene on vascular dependent platelet aggregation

ST genistein raloxifene antiplatelet platelet aggregation blood vessel

IT Blood vessel

Cardiovascular system, disease

Platelet aggregation

Platelet aggregation inhibitors

(effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT Estrogen receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT Phytoestrogens

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT 9001-84-7, Phospholipase A2 10102-43-9, Nitric oxide, biological studies 35121-78-9, Prostacyclin

RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT 446-72-0, Genistein 84449-90-1, Raloxifene

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (effect of genistein and raloxifene on vascular dependent platelet aggregation)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1/prep

PUBLISHER:

1763 L1

4449106 PREP/RL

L3 38 L1/PREP

(L1 (L) PREP/RL)

=> d 13 4 ibib abs

L3 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1180831 CAPLUS Full-text

DOCUMENT NUMBER: 145:356564

TITLE: The advance of synthetic studies on selective estrogen

receptor modulators

AUTHOR(S): Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan

CORPORATE SOURCE: ' Fourth Brigade of Pharmacy, Medical College of Chinese

People's Armed Police Force, Tianjin, 300162, Peop.

Rep. China

SOURCE: Wujing Yixueyuan Xuebao (2005), 14(2), 151-156

CODEN: WYXUA9; ISSN: 1008-5041 Wujing Yixueyuan Xuebao Bianjibu

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Chinese

AB A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl)stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

=> d 13 ibib abs 1-

YOU HAVE REQUESTED DATA FROM 38 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2007:70746 CAPLUS Full-text

DOCUMENT NUMBER: 147:172240

TITLE: Control of pharmaceuticals and animal health products

in wastewater effluents from manufacturing sites

AUTHOR(S): Parke, Neil J.; Good, Nanci F.; Meyerhoff, Roger D.

CORPORATE SOURCE: Lilly Corporate Center, Eli Lilly and Co.,

Indianapolis, IN, 46285, USA

SOURCE: WEFTEC.05, Conference Proceedings, Annual Technical

Exhibition & Conference, 78th, Washington, DC, United States, Oct. 29-Nov. 2, 2005 (2005), 145-155. Water

Environment Federation: Alexandria, Va.

CODEN: 69JOAM

DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

In many cases, the discharge of pharmaceuticals and animal health products at bulk manufacturing, fill/finish, development and research operations may not be directly regulated with numeric limitations as a part of a facility's wastewater discharge permit. The biol. activity of these discharged compds., if not properly managed, may have the potential to impact the operation of an onsite or a municipal wastewater treatment plant, aquatic species in streams, rivers, oceans, or a drinking water source. An overview of the Eli Lilly and Company environmental protection program is provided, which shows how potential releases of active ingredients from its operations are managed to protect the environment.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1063108 CAPLUS Full-text

DOCUMENT NUMBER: 145:417029

TITLE: Methods for generating stably linked complexes

composed of homodimers, homotetramers or dimers of

dimers

INVENTOR(S): Chien, Hsing Chang; Goldenberg, David M.; McBride,

William J.; Rossi, Edmund A.

PATENT ASSIGNEE(S): IBC Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT NO	•		KINI	) [	DATE		7	APPL	ICAT:	ION I	. OI		DA	ATE	
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PRIORITY APPLN. INFO.:
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                                            WO 2006-US25499
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                                            US 2006-864530P
                                                                    20061106
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The authors disclose dimerization and docking domain (DDD) sequences for the AB generation of stably tethered structures of defined compns., which may have multiple functionalities and/or binding specificities. The tethered constructs may be virtually any mol. or structure, such as antibodies, antibody fragments, antibody analogs or mimetics, aptamers, binding peptides, fragments of binding proteins, known ligands for proteins or other mols., enzymes, detectable labels or tags, therapeutic agents, toxins, pharmaceuticals, cytokines, interleukins, interferons, radioisotopes, proteins, peptides, peptide mimetics, polynucleotides, RNAi, oligosaccharides, natural or synthetic polymeric substances, nanoparticles, quantum dots, organic or inorg. compds., etc. In one example, a fusion construct of a DDD sequence with an anti-CEA Fd fragment was prepared and shown to target colorectal cancer in a xenograft model.

ANSWER 3 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2006:958171 CAPLUS Full-text

DOCUMENT NUMBER:

147:9760

TITLE:

Synthesis of raloxifene hydrochloride

AUTHOR (S):

Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong,

CORPORATE SOURCE:

Shenyang Institute of Chemical Technology, Faculty of Pharmaceutical-Engineering, Shenyang, 110142, Peop.

Rep. China

SOURCE:

AB

Zhongguo Xinyao Zazhi (2005), 14(7), 882-884

CODEN: ZXZHA6; ISSN: 1003-3734

PUBLISHER:

Zhongguo Xinyao Zazhi Youxian Gongsi

DOCUMENT TYPE:

Journal Chinese

LANGUAGE:

The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps, including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

2005:1180831 CAPLUS Full-text

DOCUMENT NUMBER:

145:356564

TITLE:

The advance of synthetic studies on selective estrogen

receptor modulators

AUTHOR (S):

Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan

CORPORATE SOURCE:

Fourth Brigade of Pharmacy, Medical College of Chinese

People's Armed Police Force, Tianjin, 300162, Peop.

Rep. China

SOURCE:

L3

Wujing Yixueyuan Xuebao (2005), 14(2), 151-156

CODEN: WYXUA9; ISSN: 1008-5041 Wujing Yixueyuan Xuebao Bianjibu

PUBLISHER: DOCUMENT TYPE:

Journal; General Review

Chinese LANGUAGE:

A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl) stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

ACCESSION NUMBER: 2005:708484 CAPLUS Full-text

DOCUMENT NUMBER: 143:221841

TITLE: Estrogen receptor ligands. Dihydrobenzoxathiin SERAMs

with an optimized antagonist side chain

AUTHOR(S): Blizzard, Timothy A.; DiNinno, Frank; Chen, Helen Y.;

Kim, Seongkon; Wu, Jane Y.; Chan, Wanda; Birzin, Elizabeth T.; Yang, Yi Tien; Pai, Lee-Yuh; Hayes, Edward C.; DaSilva, Carolyn A.; Rohrer, Susan P.;

Schaeffer, James M.; Hammond, Milton L.

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005),

15(17), 3912-3916

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:221841

AB An optimized side chain for dihydrobenzoxathiin SERAMs was discovered and attached to four dihydrobenzoxathiin platforms. The novel SERAMs show

exceptional estrogen antagonist activity in uterine tissue and an MCF-7 breast

cancer cell assay.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:451379 CAPLUS Full-text

DOCUMENT NUMBER: 142:487547

TITLE: Antiresorptive mutual salt of raloxifene and

bisphosphonic acid

INVENTOR(S): Ha, Tae Hee; Kim, Won Jeoung; Yun, Sangmin; Kim, Cheol

Kyung; Kim, Han Kyong; Suh, Kwee-Hyun; Lee, Gwan Sun

PATENT ASSIGNEE(S): Hanmi Pharm. Co., Ltd., S. Korea

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT N	10.	KI	ID DATE		API	PLICAT	ION NO.		. DAT	E
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US 20070			2007						200	60512
PRIORITY APPL			•				30494			31114
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OTHER SOURCE(S): MARPAT 142:487547

The mutual salt of raloxifene and bisphosphonic acid exhibits unexpectedly synergistic effects of two components to enhance bone mineral d. (BMD), control blood-calcium d., and lower the serum cholesterol level. For example, 3.2 g of alendronic acid was mixed with 5.0 g of raloxifene in 75 mL of ethanol/75 mL of water to obtain 6.5 g of raloxifene alendronate pentahydrate. A soft or hard capsule was prepared containing raloxifene alendronate pentahydrate 30 mg, lactose 215 mg, magnesium stearate 2 mg, and colloidal When given to female rats, the mutual salt of raloxifene and silica 3 mg. alendronic acid markedly enhanced BMD, bone stiffness, trabecular volume and bone volume, and also effectively controlled the blood cholesterol and calcium level through the synergic effects of its two components, as compared with the individual raloxifene hydrochloride or alendronate.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 7 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2004:617920 CAPLUS Full-text

DOCUMENT NUMBER:

142:463529

TITLE:

Synthesis of raloxifene hydrochloride Gong, Ping; Zhao, Yanfang; Wang, Dun

AUTHOR(S): CORPORATE SOURCE:

School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop.

Rep. China

SOURCE:

Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113

CODEN: SYDXFF; ISSN: 1006-2858

PUBLISHER:

Shenyang Yaoke Daxue Xuebao Bianjibu

DOCUMENT TYPE:

Journal Chinese

LANGUAGE:

OTHER SOURCE(S):

CASREACT 142:463529

Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3, saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR, 13C NMR.

ANSWER 8 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

2004:292022 CAPLUS Full-text

DOCUMENT NUMBER:

140:309411

TITLE:

Pharmaceutical compositions comprising raloxifene acid

addition salts and/or solvates

INVENTOR(S):

Karup, Gunnar Leo; Pedersen, Soren Bols

PATENT ASSIGNEE(S):

A/S Gea Farmaceutisk Fabrik, Den.

SOURCE:

PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004029046	A2	20040408	WO 2003-DK645	20030930
WO 2004029046	A3	20041014		

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PRIORITY APPLN. INFO.:
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OTHER SOURCE(S): MARPAT 140:309411

Raloxifene acid addn. salts or solvates thereof, having improved dissoln. properties in media comprising hydrochloric acid are described, compared with similar prepns. based on raloxifene or raloxifene-hydrochloride. The disclosed acid addition salts or solvates thereof show an improved bioavailability in media comprising hydrochloric acid, such as the gastric The acid addition salts or solvates thereof are addition salts or solvates of raloxifene and a pharmaceutically acceptable acid selected among succinic acid, lactic acid, malonic acid or sulfuric acid. Further, crystalline forms of the raloxifene salts and solvates thereof are disclosed. The raloxifene acid addition salts and/or solvates thereof are useful for the preparation of pharmaceutical composition for oral administration capable of fast and reliable release of the active ingredients in the stomach of the patient, in particular for the treatment of cancer or osteoporosis, or for inhibiting cartilage degradation A new method for preparation of raloxifene lactate is also disclosed. Thus, raloxifene malonate was prepared by the reaction of raloxifene-HCl with malonic acid in propanol-water solution The product was characterized by IR spectra and x-ray diffraction.

L3 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:269853 CAPLUS Full-text

DOCUMENT NUMBER:

140:309370

TITLE:

Amino acid and peptide carriers for oral delivery of

active agent

INVENTOR(S):

Piccariello, Thomas; Kirk, Randal J.; Olon, Lawrence

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PATENT ASSIGNEE(S):

New River Pharmaceuticals Inc., USA

SOURCE:

U.S. Pat. Appl. Publ., 176 pp., Cont.-in-part of U.S.

Pat. Appl. 2002 128,177.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

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PA	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
US	2004063628	A1	20040401	US 2002-156527	20020529
US	7060708	B2	20060613		
` WO	2000052078	A1	20000908	WO 2000-US5693	20000306

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US 2004-923257
                     A2 20040823
US 2004-953110
                     A2 20040930
US 2004-953111
                     A2 20040930
                     A2 20040930
US 2004-953116
                     A2 20040930
US 2004-953119
US 2004-955006
                     A2 20040930
WO 2004-US32131
                     A2 20040930
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The present invention relates to oral delivery systems of active agent, and more specifically to compns. that comprise amino acids, as single amino acids or peptides, covalently attached to active agents and methods for oral administration of conjugated active agent compns. For example, a polyserine-furosemide conjugate was prepared and its in vivo performance was examined Compared to parent furosemide, the conjugate showed a sustained drug release. The 9 h serum level of the polyserine-furosemide conjugate was 95.5% of its 3

h level, whereas the 9 h serum level of the parent drug was only 59.8% of its 3 h level.

L3 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:726588 CAPLUS Full-text

DOCUMENT NUMBER: 139:345292

TITLE: Nitrosation, nitration, and autoxidation of the

selective estrogen receptor modulator raloxifene by

nitric oxide, peroxynitrite, and reactive

nitrogen/oxygen species

AUTHOR(S): Toader, Violeta; Xu, Xudong; Nicolescu, Adrian; Yu,

Linning; Bolton, Judy L.; Thatcher, Gregory R. J.

CORPORATE SOURCE: Department of Medicinal Chemistry and Pharmacognosy,

College of Pharmacy, University of Illinois at

Chicago, Chicago, IL, 60612-7231, USA

SOURCE: Chemical Research in Toxicology (2003), 16(10),

1264-1276

CODEN: CRTOEC; ISSN: 0893-228X

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

The regulation of estrogenic and antiestrogenic effects by selective estrogen AB receptor modulators (SERMs) provides the basis for use in long-term therapy in cancer chemoprevention and postmenopausal osteoporosis. However, the evidence for carcinogenic properties within this class requires study of potential pathways of toxicity. There is strong evidence for the elevation of cellular levels of NO in tissue treated with SERMs, including the benzothiophene derivative, raloxifene, in part via up-regulation of nitric oxide synthases. Therefore, the reactions of  $17\beta$ -estradiol (E2), raloxifene, and an isomer with NO, peroxynitrite, and reactive nitrogen/oxygen species (RNOS) generated from NO2-/H2O2 systems were examined Peroxynitrite from bolus injection or slow release from higher concns. of 3-morpholinosydnonimine (SIN-1) reacted with the benzothiophenes and E2 to give aromatic ring nitration, whereas peroxynitrite, produced from the slow decomposition of lower concns. of SIN-1, was relatively unreactive toward E2 and yielded oxidation and nitrosation products with raloxifene and its isomer. The oxidation and nitrosation products formed were characterized as a dimer and quinone oxime derivative Interestingly, the reaction of the benzothiophenes with NO in aerobic solution efficiently generated the same oxidation products. Stable quinone oximes are not unprecedented but have not been previously reported as products of RNOSmediated metabolism The reaction of glutathione (GSH) with the quinone oxime gave both GSH adducts from Michael addition and reduction to the corresponding o-aminophenol. The ready autoxidn. of raloxifene, observed in the presence of NO, is the first such observation on the reactivity of SERMs and is potentially a general phenomenon of significance to SERM chemical toxicol.

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:491620 CAPLUS Full-text

DOCUMENT NUMBER: 139:179942

TITLE: Synthesis of Constrained Raloxifene Analogues by

Complementary Use of Friedel-Crafts and Directed

Remote Metalation Reactions

AUTHOR(S): Kalinin, Alexey V.; Reed, Mark A.; Norman, Bryan H.;

Snieckus, Victor

CORPORATE SOURCE: Department of Chemistry, Queen's University, Kingston,

ON, K7L 3N6, Can.

SOURCE: Journal of Organic Chemistry (2003), 68(15), 5992-5999

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal English LANGUAGE:

CASREACT 139:179942 OTHER SOURCE(S):

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

New constrained heterocyclic analogs of Raloxifene, I [R1 = 2-(1-AΒ piperidinyl)ethoxy, R2 = H; R1 = H, R2 = 2-(1-piperidinyl)ethoxy] and II, were prepared by complementary Directed remote Metalation (DreM)/Friedel-Crafts cyclization approaches. Utilization of a benzylidene-thiolactone rearrangement was successfully implemented to construct benzothiophenes III (R3 = Me2CH, R4 = MeO; R3 = Me, PhCH2, R4 = Et2N) in good yields. Selective deprotection of III (R3 = Me2CH, R4 = MeO; R3 = PhCH2, R4 = Et2N) induced by complexation was followed by trifluoromethylsulfonylation and Suzuki-Miyaura cross coupling with 3-[2-(1-piperidinyl)ethoxy]phenyl dioxaborolane to give the corresponding 2,4-diaryl-substituted benzothiophenes with methoxycarbonyl or diethylcarbamoyl group in the 3 position. Treatment of the latter with BC13 or with excess LDA induced an intramol. para or ortho cyclization and concomitant double deprotection to furnish I. Similar sequence starting from III (R3 = Me, R4 = Et2N) afforded the constrained analog II.

REFERENCE COUNT:

30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 12 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

2002:408662 CAPLUS Full-text

DOCUMENT NUMBER:

136:401637

TITLE:

Preparation of 3-arylbenzothiophenes by

cyclodehydration of phenylthioacetophenones using

activated clay or zeolite catalysts.

INVENTOR(S):

Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA PCT Int. Appl.; 26 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	CENT 1	NO.			KIN	D :	DATE	-4-	2	APPL	ICAT:	ION I	NO.	•	D	ATE	
WO	2002	0422	 89		A2	-	2002	0530	1	WO 2	001-1	US42	940		2	0011	114
WO	2002	0422	89		<b>A3</b>		2002	0906									
WO	2002	0422	89		<b>A8</b>		2004	0212				•					
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JΡ,	ΚE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PH,	PL,
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,
		US,	UZ,	VN,	ΥU,	ZA,	ZW										
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AM,	AZ,	BY,	KG,
		KZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	CH,	CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,
		IE.	IT.	LU.	MC.	NL.	PT.	SE.	TR.	BF.	BJ.	CF.	CG.	CI,	CM.	GA,	GN.

GQ, GW, ML, MR, NE, SN, TD, TG

A5 20020603 AU 2002-30409 AU 2002030409

US 2004132775 A1 20040708 US 2003-415569 20030922

US 6921827 B2 20050726

PRIORITY APPLN. INFO.: US 2000-253212P P 20001127

WO 2001-US42940 W 20011114

OTHER SOURCE(S): CASREACT 136:401637; MARPAT 136:401637

$$R^{10}$$
 $R^{10}$ 
 $R^{10}$ 

Title compds. (I; R1, R2 = H, protecting group) were prepd. by cyclodehydration of phenylthioacetophenones (II; variables as above) in the presence of acid activated clays or acid activated zeolites and in the presence of solvents. Thus, PhMe, α-(3-methoxyphenylthio)-4-methoxyacetophenone, and "acid-activated clay" (Engelhard X-9107) were combined and refluxed 2 h using a Dean Stark trap. By HPLC the product mixture consisted of 96.7% 6-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, 1.1% 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene, 2.1% 4-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, and 0.1% 4-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene.

L3 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:408636 CAPLUS Full-text

DOCUMENT NUMBER: 136:401533

TITLE: Coupling reaction process for preparing

 $\alpha$ -(3-arylthio)acetophenones from thiophenol derivs. and  $\alpha$ -(leaving group)-substituted

acetophenones

INVENTOR(S): Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

OCCUMENT TYPE: Patent

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATE	I T	10.			KIN	D	DATE			APPL	ICAT:	ION I	. 01		D	ATE	
						-											
WO 20	020	1422	51		A2		2002	0530	. ,	WO 2	001-1	JS42	939		20	0011	114
WO 20	0020	1422	51		<b>A3</b>		2003	0306									
V	<b>V</b> :	ΑE,	AG,	AL,	AM,	ΑT,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	CZ,	DE,	DE,	DK,	DK,	DM,	DZ,	EC,	EE,	EE,	ES,
		FI,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,
		KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,
		MX,	MZ,	NO,	NZ,	PH,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SK,	SL,
		TJ,	TM,	TR,	TT,	TZ,	ÜΑ,	ŪĠ,	US,	UZ,	VN,	ΥU,	ZA,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU												
F	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM; GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002028593 A5 20020603 AU 2002-28593 20011114 PRIORITY APPLN. INFO.: US 2000-253073P P 20001127

WO 2001-US42939 W 20011114

OTHER SOURCE(S): CASREACT 136:401533; MARPAT 136:401533

GI

$$R^1 = 0$$
  $S \longrightarrow 0 = R^2$ 

AB  $\alpha$ -(3-Arylthio)acetophenones [I; R1, R2 = H, hydroxy-protecting group; e.g.,  $\alpha$ -(3-methoxyphenylthio)-4-methoxyacetophenone] are prepared in high yield and selectivity by the coupling of a thiophenol derivative 3-(R1O)C6H4SH (e.g., 3-methoxybenzenethiol) in an aqueous alkaline (e.g., KOH) solvent (e.g., Et acetate) with an aromatic ketone LCH2COC6H4(OR2)-4 (L = leaving group; e.g.,  $\alpha$ -chloro-4-methoxyacetophenone).

L3 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:283971 CAPLUS Full-text

DOCUMENT NUMBER: 134:300772

TITLE: Glycosides and orthoester glycosides of raloxifene and

analogues and the use thereof

INVENTOR(S): Holick, Michael Francis; Ramanathan, Halasya

PATENT ASSIGNEE(S): Strakan Group PLC, UK SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		D	ATE	
					_									_	-'	
WO 200:	10271	29		<b>A1</b>		2001	0419	1	WO 2	000-	GB38	64		2	0001	006
W:	AE,	AG,	AL,	AM,	ΑŢ,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN.,
	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,
•	НU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,
•	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,
	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VN,
	ΥU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM				
RW	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	ΑT,	BE,	CH,	CY,
	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PΤ,	SE,	BF,	ΒJ,
	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
GB 2359		Α		2001	0411	(	GB 1	999-	2810	0		1:	9991	126		
PRIORITY API	PRIORITY APPLN. INFO.:							1	US 1	999-	1581	41P		P 1	9991	800
	RIORIII APPUN. INFO.:							1	US 2	000-	2315	73P		P 2	0000	911
A	. (			***	~ ~ ~											

OTHER SOURCE(S): MARPAT 134:300772

AB Raloxifene and raloxifene analog glycosides and orthoester glycosides afford greater serum bioavailability of the hydroxylated parent compound, and are useful for treating or preventing a number of conditions that may be treated with an anti-estrogenic or an anti-androgenic compound To a mixture of 0.5 g

raloxifene and 1.6 g silvér silicate in dry acetonitrile was added 3 g mol. sieves and stirred for 20 min. To the above suspension was added 1.0 g acetobromo- $\alpha$ -D-glucose and heated for 2 h at 60°, then filtered through a bed of silica gel and eluted with dichloromethane and methanol. The yellow eluent was concentrated under vacuum to obtain yellowish crystals. Proton NMR spectrum showed the crystals were consisted of 2 possible monoglucosides and a doubly glycosylated product.

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2007 ACS on STN L3 ANSWER 15 OF 38 1999:440767 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER: 131:228604

TITLE: Synergistic methodologies for the synthesis of

3-aroyl-2-arylbenzo[b] thiophene-based selective

estrogen receptor modulators. Two concise syntheses of

raloxifene

Bradley, David A.; Godfrey, Alexander G.; Schmid, AUTHOR (S):

Christopher R.

Chemical Process Research and Development, A Division CORPORATE SOURCE:

> of Eli Lilly and Company, Lilly Corporate Center, Lilly Research Laboratories, Indianapolis, IN,

46285-4813, USA

Tetrahedron Letters (1999), 40(28), 5155-5159 SOURCE:

CODEN: TELEAY; ISSN: 0040-4039

Elsevier Science Ltd. PUBLISHER:

Journal DOCUMENT TYPE: LANGUAGE: English

Functionalized benzo[b] thiophene intermediates are prepd. which allow fully ΔR independent elaboration of the 2-aryl position or the tether position of benzo[b]thiophene-based selective estrogen receptor modulators (SERMs). Two

concise syntheses of the SERM raloxifene (Evista) are presented.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 16 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

1999:188589 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER: 130:311683

Novel nonsteroidal selective estrogen receptor TITLE:

> modulators. Carbon and heteroatom replacement of oxygen in the ethoxypiperidine region of raloxifene

Schmid, Christopher R.; Sluka, James P.; Duke, Kristen AUTHOR(S):

M.; Glasebrook, Andrew W.

Lilly Research Laboratories, A Division of Eli Lilly CORPORATE SOURCE:

and Company, Lilly Corporate Center, Indianapolis, IN,

46285, USA

Bioorganic & Medicinal Chemistry Letters (1999), 9(4), SOURCE:

523-528

CODEN: BMCLE8; ISSN: 0960-894X

Elsevier Science Ltd. PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

Compds. were synthesized where oxygen in the ethoxypiperidine region of AB raloxifene is replaced with carbon, sulfur, or nitrogen linkages. Thia- and aza-substituted compds. were prepared by novel methodol. The compds. were evaluated in vitro as selective estrogen receptor modulators (SERMs). Calcns. suggested the compds. exhibit an ER- $\alpha$  binding affinity/conformational energy relationship.

THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 31 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 17 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

1999:71534 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER: 130:196550

Nucleophilic aromatic substitution on TITLE:

> 3-aroyl-2-arylbenzothiophenes. Rapid access to raloxifene and other selective estrogen receptor

modulators

Schmid, Christopher R.; Sluka, James P.; Duke, Kristin AUTHOR (S):

Lilly Research Laboratories, A Division of Eli Lilly CORPORATE SOURCE:

and Company, Lilly Corporate Center, Indianapolis, IN,

46285-4813, USA

Tetrahedron Letters (1999), 40(4), 675-678 SOURCE:

CODEN: TELEAY; ISSN: 0040-4039

Elsevier Science Ltd. PUBLISHER:

Journal DOCUMENT TYPE: English LANGUAGE:

CASREACT 130:196550 OTHER SOURCE(S):

Versatile, mild and high yielding methods for nucleophilic arom. substitution

of 2-dialkylamino-1-ethoxides and related nucleophiles on 3-aroyl-2-

arylbenzothiophene nuclei are presented. A short synthesis of raloxifene is

detailed.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 18 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1998:721690 CAPLUS Full-text

DOCUMENT NUMBER:

130:3769

TITLE:

Processes for preparing benzothiophenes

INVENTOR(S):

McGill, John McNeil, III; Misner, Jerry Wayne; Zhang,

Tony Yantao

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PA	TENT :				KINI	)	DATE			APPL	ICAT	ION I	NO.		D	ATE	
		'-				-									-		
WO	9849	156			A1		1998	1105		WO 1	998-1	US85	09		1:	9980	428
	W:	AL,	AM,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CN,	CU,	CZ,	EE,	GE,	GH,
		GM,	GW,	HU,	ID,	IL,	IS,	JΡ,	KE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,
		LT,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	RO,	RU,	SD,	SG,	SI,
		SK,	SL,	TJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,	ΥU,	ZW			
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
		GN,	ML,	MR,	NE,	SN,	TD,	TG			•						
CA	2287	943			A1		1998	1105	· (	CA 1	998-	2287	943		1:	9980	128
AU	9872	613			Α		1998	1124		AU 1	998-	7261	3		1	9980	128
BR	9809	439			Α		2000	0613	]	BR 1	998-	9439			1	9980	128
HU	2000	0318	7		A2		2001	0528	]	HU 2	000-3	3187			1:	99804	128
JP	2001	5223	72		T		2001	1113	,	JP 1	998-	5472	77		1	99804	128
US	6090	949			Α		2000	0718	1	US 1	998-	6949	7		1	9980	129
EP	8755	10			<b>A1</b>		1998	1104	]	EP 1	998-	3033	74		1:	9980	430
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO										
MX	9909	883			Α		2000	0331	]	MX 1	999-	9883			1:	9991	027
PRIORIT	Y APP	LN.	INFO	. :					1	US 1	997-	4517	7 P	1	2 1:	99704	130

OTHER SOURCE(S): CASREACT 130:3769; MARPAT 130:3769

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compds. [I; Y = Cl, Br, I, SO2(Cl-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = Cl-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.

REFERENCE COUNT:

4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1998:721501 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER:

130:3768

TITLE:

Demethylation process for preparing benzo[b]thiophenes

Hoard, David Warren; Luke, Wayne Douglas

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA Eur. Pat. Appl., 13 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

INVENTOR(S):

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT N	10.	KIND	DATE	APPLICATION NO.	DATE
EP 87551	L <b>1</b> .	A1	19981104	EP 1998-303345	19980429
R:	AT, BE, CH,	DE, DE	, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,
	IE, SI, LT,	LV, FI	, RO		
CA 22362	254	A1	19981030	CA 1998-2236254	19980427
JP 11005	5789	Α	19990112	JP 1998-118628	19980428
US 59945	547	Α	19991130	US 1998-69500	19980429
PRIORITY APPI	N. INFO.:			US 1997-45156P	P 19970430
OTHER SOURCE	(S):	CASREA	CT 130:37	68; MARPAT 130:3768	
GI				•	

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$$\begin{array}{c|c}
0 & N & R^1 \\
\hline
 & R^2 & \\
\hline
 & R^2$$

AB The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be carried out in the same reaction vessel without isolation of the acylated, protected material.

REFERENCE COUNT:

10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:719257 CAPLUS Full-text

DOCUMENT NUMBER:

130:3765

TITLE:

Intermediates and processes for preparing

benzo[b] thiophenes

INVENTOR(S):

Misner, Jerry Wayne; Schmid, Christopher Randall

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 1

PAT	TENT 1	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		D	ATE	
						-									_		
WO	9848	793			A1	•	1998	1105	1	WO 1	998-1	US85	10		1	9980	428
	W:	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
		DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	GW,	HU,	ID,	IL,	IS,	JP,	KΕ,	KG,
		ΚP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
		NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,
		UA,	UG,	US,	UZ,	VN,	ΥU,	ZW								•	
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SZ,	ŪĠ,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,
		FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	BJ,	CF,	CG,	CI,
		CM,	GΑ,	GN,	ML,	MR,	NE,	SN,	TD,	TG							
CA	2287	922			A1		1998	1105	(	CA 1:	998-	2287	922		19	9980	428
ΑU	9872	614			A		1998	1124	7	AU 1	998-	7261	4		1:	980	428
ΕP	9790	76			A1		2000	0216	]	EP 1:	998-	9199	36		1:	9980	428
	R:	ΑT,	BE,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	NL,	SE,	PT,	ΙE,	FI		
JP	2001	5232	53		T		2001	1120	1	JP 1:	998-	5472	78		1:	9980	428
US	6018	056			Α		2000	0125	1	US 1:	998-	6927	8		19	9980	429

US 1997-45131P P 19970430 PRIORITY APPLN. INFO.:

WO 1998-US8510 W 19980428

OTHER SOURCE(S):

CASREACT 130:3765; MARPAT 130:3765

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

ÀΒ The title compds. [I-III; R = hydroxy protecting group; Y = CO2H, CO2(C1-4 alkyl), C(halo), etc.; A = OH, halo, NO2, etc.; R1 = hydroxy protecting group, H], useful intermediates in the further preparation of pharmaceutical benzo[b]thiophenes, were prepared Thus, reaction of 6-methoxythianaphthen-2one with p-anisaldehyde in the presence of piperidine in EtOH and THF afforded 45% E/Z-I [R = Me].

REFERENCE COUNT: THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 21 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1998:161136 CAPLUS Full-text

DOCUMENT NUMBER:

128:221639

TITLE:

Preparation of amorphous benzothiophenes for

pharmaceuticals

INVENTOR (S):

Cuff, George W.; Thakkar, Arvind L.

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA; Cuff, George W.; Thakkar,

Arvind L.

SOURCE:

PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PA?	TENT NO. KIND DATE								i	APP	LICA	TION	ΝĢ.		D.	ATE	
WO	9808	513			A1	<b>-</b> -;	 1998	0305	. 1	 WO	1997	 -US14	768		1	 9970	822
	W:	AL,	AM,	AU,	AZ,	BA,	BB,	BG,	BR,	BY	, CA	, CN,	CU,	CZ,	EE,	GE,	GH,
		HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ	LC	, LK,	LR,	LT,	LV,	MD,	MG,
		MK,	MN,	MW,	MX,	NO,	NZ,	PL,	RO,	RU	, SD	, SG,	SI,	SK,	SL,	TJ,	TM,
								VN,									
	RW:	GH,	KΕ	LS,	MW,	SD,	SZ,	UG,	ZW,	ВF	, BJ	, CF,	CG,	CI,	CM,	GA,	GN,
								-									
ΕP	8266	82	·	•	A1		1998	0304	1	EΡ	1997	-3064	26		1	9970	822
ΕP	8266	82			В1	:	2003	0312									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT	, LI,	LU,	NL,	SE,	MC,	PT,
		-	-	-	LV,			•	·		•		·	·	·	•	·
CA	2263	175	•	·	A1		1998	0305	(	CA	1997	-2263	175		1	9970	822
AU	9742	335		,	Α		1998	0319	. ;			-4233				9970	
	7239																
IN	1829	40			A1		1999	0814		IN	1997	-CA15	49		. 1	9970	822
BR	9713	176			Α	:	2000	0208				-1317				9970	
CN	1244	124			Α		2000	0209		CN	1997	-1974	34		1	9970	822
HU	2000	0117	2		A2		2001	0628	]	HU	2000	-1172			1	9970	822
HU	2000	0117			A3		2002	0128									
	3338				A		2001	0629	j	NZ	1997	-3338	39		1	9970	822
	1286						2001	1031				-1286				9970	
TR	9900	403			<b>T</b> 2	:	2002	0121	,	TR	1999	-403			1	9970	822
JP	2002	5141			Т		2002	0514		JP	1998	-5117	44		1	9970	822
	2342				·T			0315				-3064				9970	822
					_	•			-							- · •	

ES 1997-306426 19970822 ES 2195089 T3 20031201 ZA 1997-7617 19990225 19970825 ZA 9707617 Δ 19970825 US 6713494 · B1 20040330 US 1997-918741 NO 9900914 19990225 NO 1999-914 19990225 Α 20000626 KR 1999-701682 19990227 KR 2000035941 Α US 1996-24831P P 19960828 PRIORITY APPLN. INFO.: W 19970822 WO 1997-US14768

OTHER SOURCE(S): MARPAT 128:221639

A method for prepq. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS 1 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 22 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3 1997:589698 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

127:272904

TITLE:

Evaluation of piperidinoethoxy moiety as an antiestrogenic substituent in non-steroidal

anti-estrogens: fertility regulation

AUTHOR (S):

Tripathi, Sachi; Dwivedy, Indra; Dhar, J. D.; Dwivedy,

Anila; Ray, Suprabhat

CORPORATE SOURCE:

Medicinal Chemistry Division, Central Drug Research

Institute, Lucknow, 226 001, India

SOURCE:

Bioorganic & Medicinal Chemistry Letters (1997),

7(16), 2131-2136

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: DOCUMENT TYPE: Elsevier Journal

LANGUAGE: English AB

A piperidinoethoxy substituent in non-steroidal antiestrogens has a relatively higher antiestrogenic effect as compared to a pyrrolidinoethoxy moiety. However, the antagonistic activity is more depended on the mol. geometry than the nature of the basic chain. No significant difference in the antifertility activity in these two sets of compds. was observed

REFERENCE COUNT:

12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 23 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1997:124440 CAPLUS Full-text

DOCUMENT NUMBER:

126:144105

TITLE:

Preparation of 3-phenylbenzo[b]thiophenes

Hoard, David W.; Luke, Wayne D. INVENTOR(S):

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA; Hoard, David W.; Luke, Wayne

SOURCE:

PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 9640677	A1 19961219	WO 1996-US9477	19960604
W: AL, AM, AT,	AU, AZ, BB, BG,	BR, BY, CA, CH, CN, CZ,	DE, DK, EE,

```
ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
             LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
             SE, SG
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
                                 19970225
                                             US 1995-481015
                                                                     19950607
     US 5606075
                          Α
                                             CA 1996-2223709
                                                                     19960604
     CA 2223709
                          A1
                                 19961219
                                             AU 1996-61010
     AU 9661010
                          Α
                                 19961230
                                                                     19960604
     AU 703017
                                 19990311
                          B2
     EP 830355
                          A1
                                 19980325
                                             EP 1996-918320
                                                                     19960604
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
             SI, LT, LV, FI
                                             CN 1996-196109
     CN 1192738
                          Α
                                 19980909
                                                                     19960604
     BR 9608851
                          Α
                                 19990608
                                             BR 1996-8851
                                                                     19960604
     JP 11507347
                          T
                                 19990629
                                             JP 1996-501787 .
                                                                     19960604
     HU 9900898
                          A2
                                 19990728
                                             HU 1999-898
                                                                     19960604
     HU 9900898
                          A3
                                 20000228
                                 20010418
                                             EP 2000-128207
                                                                     19960604
     EP 1092714
                          A2
     EP 1092714
                          A3
                                 20010704
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
             SI, LT, LV, FI
                                             IL 1996-122128
     IL 122128
                          Α
                                 20010808
                                                                     19960604
     NO 9705627
                          Α
                                 19980127
                                             NO 1997-5627
                                                                     19971204
PRIORITY APPLN. INFO.:
                                             US 1995-481015
                                                                  A 19950607
                                             EP 1996-918320
                                                                  A3 19960604
                                             WO 1996-US9477
                                                                  W
                                                                     19960604
                         MARPAT 126:144105
OTHER SOURCE(S):
```

$$R^1$$
  $R^2$ 

GI

L3

AB Title compds. [I; R1,R2 = H, halo, (aryl)alkoxy, NH2] were pred. by cyclization of 4-R1C6H4CH:C(SR4)C6H4R2-4 [R4 = trialkylsilyloxy, (di)(alkyl)amino, alkylthio, etc.] in the presence of an acid.

```
1996:740256 CAPLUS Full-text
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         126:7985
TITLE:
                         Preparation of 3-[4-(2-heterocyclylethoxy)benzoyl-2-
                         phenylbenzothiophenes for use in alleviating the
                         symptoms of post-menopausal syndrome
                         Dodge, Jeffrey Alan; Jones, Charles David; Bourgeois,
INVENTOR(S):
                         Tokarz Michelle Lee
                         Eli Lilly and Co., USA
PATENT ASSIGNEE(S):
SOURCE:
                         Eur. Pat. Appl., 67 pp.
                         CODEN: EPXXDW
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
```

CAPLUS COPYRIGHT 2007 ACS on STN

FAMILY ACC. NUM. COUNT: 1

ANSWER 24 OF 38

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

EP 738725 Ά2 19961023 EP 1996-302713 19960418 EP 738725 A3 19970305 R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, NL, PT, SE US 6608090 В1 20030819 US 1995-426552 19950421 CA 2215902 CA 1996-2215902 19960418 A1 19961024 WO 9632937 WO 1996-US5382 19960418 **A1** 19961024 AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, US, UZ RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 1996-55549 AU 9655549 Α 19961107 19960418 Т 19960418 JP 11504013 19990406 JP 1996-531911 PRIORITY APPLN. INFO.: US 1995-426339 19950421 US 1995-426552 19950421 19960418 WO 1996-US5382

OTHER SOURCE(S): MARPAT 126:7985

$$R^{2}$$
 $R^{2}$ 
 $R^{2$ 

The title compds. [I; R1, R2 = H, OH, alkoxy, etc.; R3 = (substituted) pyrrolidino, piperidino, piperazino, etc.], useful in alleviating the symptoms of post-menopausal syndrome related to osteoporosis, cardiovascular disease, hyperlipidemia, estrogen-dependent cancer, and in alleviating the symptoms of uterine fibroid disease, endometriosis, aortal smooth muscle cell proliferation, and restenosis, were prepared and formulated. Thus, reaction of bromide II with 3-phenylpyrrolidine in DMF followed by demethylation with EtSH/AlCl3 in CH2Cl2 afforded I [R1, R2 = H; R3 = 3-Ph-pyrrolidin-1-yl] which reduced 63.4% serum cholesterol at 10 mg/kg.

L3 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1996:672963 CAPLUS Full-text

DOCUMENT NUMBER: 126:7983

TITLE: Process for the synthesis of benzo[b] thiophenes

INVENTOR(S): Hoard, David W.; Luke, Wayne D. PATENT ASSIGNEE(S): Eli Lillŷ and Company, USA

SOURCE: U.S., 10 pp.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

English

PATENT INFORMATION:

	TENT																
	5569																
	2223																
WO	9640	678			A1		1996	1219		WO	1996	-US93	57		1	9960	604
	W:	AL,	AM,	AT,	AU,	AZ,	ВВ,	BG,	BR,	BY	, CA	, CH,	CN,	CZ,	DE,	DK,	EE,
		ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE	, KG	, KP,	KR,	KZ,	LK,	LR,	LS,
		LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX	, NO	, NZ,	PL,	PT,	RO,	RU,	SD,
		SE,	SG														
	RW:	KE,	LS,	MW,	SD,	SZ,	ŪĠ,	ΑT,	BE,	CH	, DE	, DK,	ES,	FI,	FR,	GB,	GR,
		ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ	, CF	, CG,	CI,	CM,	GA	•	
AU	9660	970			Α		1996	1230		ΑU	1996	-6097	0		1	9960	604
AU	6985	58			B2		1998	1029									
	8303									EΡ	1996	-9182	77		1	9960	604
EP	8303	56			В1		2001	0822									
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT	, LI,	LU,	NL,	SE,	PT,	IE,
٠		SI,	LT,	LV,	FI												
	1192						1998	0902		CN	1996	-1958	99		1	9960	604
BR	9609 1150	156			Α		1999	0629		BR	1996	-9156			1	9960	604
							1999	0629		JΡ	1997	-5016	94		1	9960	604
HU	9900	903			A2		1999	0728		HU	1999	-903			1	9960	604
	9900				<b>A3</b>		2001	0129									
	1220						2001	0520		$\mathbf{IL}_{\cdot}$	1996	-1220	91		1	9960	604
AT	2045	75			T		2001	0915		AΤ	1996	-9182	77		1	9960	604
ES	2159 8303	742			Т3		2001	1016		ES	1996	-9182	77		1	9960	604
PT	8303	56			T		2001	1228		PT	1996	-9182	77		1	9960	604
NO	9705	579			Α		1997	1203		NO	1997	-5579			1	9971:	203
PRIORITY	Y APP	LN.	INFO	. :								-4868					
												-US93.		I	W 1	9960	604
OTHER SO	OURCE	(S):			CASI	REAC	T 12	6:798	33;	MAR	PAT :	126:7	983				
GI																	

$$R^{1}$$
 $R^{2}$ 
 $R^{2}$ 

The title compds. I [R1, R2 = H, alkoxy, etc.] are prepd. Thus, treatment of AB (E) -tert-Bu 4,4'-dimethoxystilbenyl sulfoxide with p-toluenesulfonic acid in refluxing toluene gave, after workup and purifn, (E) - and (Z) -I [R1 = R2 = MeO].

L3 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:649600 CAPLUS Full-text

DOCUMENT NUMBER: 125:266032

TITLE: Phosphorous-containing benzothiophenes, their

preparation, their use in treating postmenopausal

syndrome-associated indications and estrogen-dependent

diseases, and pharmaceuticals containing them

INVENTOR(S): Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey

S.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
EP 729964	A1	19960904	EP 1996-300878	19960209		
EP 729964	B1 .	20010509				
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IE, IT, LI, LU,	NL, PT, SE		
US 6479517	B1	20021112	US 1995-395944	19950228		
ES 2158242	<b>T</b> 3	20010901	ES 1996-300878	19960209		
CA 2169414	A1	19960829	CA 1996-2169414	19960213		
JP 08259560	Α	19961008	JP 1996-25281	19960213		
US 5998443	A	19991207	US 1997-946842,	19971008		
PRIORITY APPLN. INFO.:			US 1995-395944 I	19950228		
OTHER SOURCE(S):	MARPAT	125:266032				
GI						

Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(0-alkyl)2, OPO(0-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds.

of the invention, as well as pharmaceutical compns. containing compds. of the invention.

ANSWER 27 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:333087 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER:

125:86485

TITLE:

Prepn. of vinyl sulfenic acid derivatives for

benzo[b] thiophene synthesis Hoard, David W.; Luke, Wayne D.

INVENTOR(S):

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 13 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	CENT 1						DATE										ATE 	
	us	5514						1996										9950	•
	CA	2224	225			A1	•	1996	1219		CA	199	96-2	2224	225		1	9960	604
	WO	9640	693			A1		1996	1219		WO	199	96-T	JS94	50		1	9960	604
		W:	AL,	AM,	AT,	AU,	ΑZ,	BB,	BG,	BR,	BY	?, (	CA,	CH,	CN,	CZ,	DE,	DK,	EE,
			ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE	E, I	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LS,
			LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX	(, l	, OI	NZ,	PL,	PT,	RO,	RU,	SD,
•			SE,	SG															
		RW:	KE,	LS,	MW,	SD,	SZ,	ŪĠ,	ΑT,	BE,	CH	I, I	DΕ,	DK,	ES,	FI,	FR,	GB,	GR,
			ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ΒJ	τ, (	CF,	CG,	CI,	CM			
	ΑU	9661	003			Α		1996	1230		AU	199	96-6	5100	3		1	9960	604
	ΑU	6980	76			B2		1998	1022										
	EΡ	8303	62			A1		1998	0325		ΕP	199	96-9	9183	14		1	9960	604
							•	ES,		•		•	•	•	•	•	•	PT,	ΙE,
		11922	SI,	LT,	LV,	FΙ													
	CN	11922	215			· A		1998	0902		CN	199	96-3	19594	17		1	9960	604
		10688						2001											
	BR	96088	847			Α		1999	0608		BR	199	96-8	3847			1	9960	604
1	JP	1150	7346			T		1999	0629		JP	199	97-5	5017	74		1	9960	604
:	HU	99009	923			A2		1999	0728		HU	199	99-9	923			1	9960	604
		99009						2000	0228										
		12212						2001	0520		ΪL	199	96-:	1221:	27·		1	9960	604
1	МО	9705	633 .			Α		1998	0128					5633				9971	204
•	CN	13300	071			Α		2002	0109					1307				0001	
PRIOR	ITY	APPI	LN.	INFO	.:									1826					
		-												1836					
										,	WO	199	96-ĭ	JS946	50	1	W 1	9960	604

GI

$$R^1$$
 CH  $=$   $CH$   $=$   $R^2$ 

The present invention is directed to novel vinyl sulfenic acid derivs. I [R1, AB R2 = H, alkoxy, arylalkoxy, halo, amino; R4 = OSi(R3)3, NR5R6, SR8; R5and/or R6 = H, alkyl, arylalkyl, aryl, -(CH2)5-, -(CH2)4-, -(CH2)2O(CH2)2-, -(CH2)6-; R8 = alkyl, aryl, arylalky] useful for the synthesis of benzo[b]thiophenes, in particular 2-arylbenzo[b]thiophenes. E.g., desoxyanisoin reacts with 2-methyl-2-propanethiol to give I [R1 = R2 = OMe; R4 = C(Me)3] which in turn cyclizes to 6-methoxy-2-(4- methoxyphenyl)benzo[b]thiophene.

ANSWER 28 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

1996:256454 CAPLUS Full-text

DOCUMENT NUMBER:

124:289252

TITLE:

Process for preparing benzoic acid derivative

intermediates and benzothiophene pharmaceutical agents

INVENTOR (S): PATENT ASSIGNEE(S): Kjell, Douglas Patton Eli Lilly and Co., USA

Eur. Pat. Appl., 16 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 699673	A1	19960306	EP 1995-306053	19950830
EP 699673	B1	19980422	•	
R: AT, BE, CH,	DE, DK	, ES, FR,	GB, GR, IE, IT, LI, LU,	NL, PT, SE
US 5731436	A	19980324	US 1994-298891	19940831
IL 115091	Α	20000831	IL 1995-115091	19950828
IL 126593	A	20000831	IL 1995-126593	19950828
CA 2157235	A1	19960301	CA 1995-2157235	19950830
FI 9504068	A	19960301	FI 1995-4068	19950830
HU 73136	A2	19960628	HU 1995-2539	19950830
BR 9503847	Α	19960917	BR 1995-3847	19950830
AT 165356	T	19980515	AT 1995-306053	19950830
ES 2114722	<b>T</b> 3	19980601	ES 1995-306053	19950830
JP 08119912	A	19960514	JP 1995-223184	19950831
US 5955608	A	19990921	US 1998-16761	19980130
PRIORITY APPLN. INFO.:			US 1994-298891	A 19940831
			IL 1995-115091	A3 19950828
OTHER SOURCE(S):	MARPAT	124:28925	52	

OTHER SOURCE(S):

GI

$$O(CH_2)$$
  $nNR1R2$ 
 $O(CH_2)$   $nNR1R2$ 
 $OR4$ 
 $OR$ 

The present invention provides a novel process for prepg. a compd. of formula AB RO2C(p-C6H4)O(CH2)nNR1R2 [R = C1-C4 alkyl; R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino,

morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3]; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2(p-C6H4)O(CH2)nOH [R and n are as defined above, with a leaving group donor]; and (c) reacting the product of step (b), a compound of formula RO2(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneamine]. The product of the above process also is novel and is useful for the preparation of pharmaceutically active compds. of formula I, particularly via the following novel process [R = C1-C4 alkyl; R1 and R2 each are independently C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino, morpholino, dimethylamino, diethylamino, of 1-hexamethyleneimino; n = 2, 3; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2C(p-C6H4)O(CH2)nOH [R and n are as defined above, with the leaving group donor]; (c) reacting the product of step (b), a compound of formula RO2C(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneimine]; (d) reacting the product of step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing the reaction product from step (d); and (f) optionally forming a salt of the reaction product from either step (d) or step (e).

L3 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1996:237478 CAPLUS Full-text

DOCUMENT NUMBER:

124:289249

TITLE:

An improved process for preparing 3-(4-

aminoethoxybenzoyl) benzo[b] thiophenes

INVENTOR(S):

Alt, Charles Arthur Eli Lilly and Co., USA

PATENT ASSIGNEE(S): SOURCE:

Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT:

PA:	TENT NO.			KINI	)	DATE		API	PLICAT	ION I	NO.		D	ATE	
					-										
EP	693488			A1		1996	0124	EP	1995-	3050	85		19	9950	720
EP	693488			B1		2001	0919								
	R: AT,	BE,	CH,	DE,	DK	, ES,	FR,	GB, GF	R, IE,	IT,	LI,	LU,	NL,	PT,	SE
US	5523416			Α		1996	0604	US	1995-	4222	94		19	9950	414
HU	71596			A2		1996	0129	HU	1995-	2176			19	9950'	719
ΑU	9525068			Α		1996	0201	AU	1995-	2506	8		19	9950	719
AU	684181			B2		1997	1204								
ZA	9506031			Α		1997	0120	ZA	1995-	6031			19	9950	719
CA	2154319			A1		1996	0123	CA	1995-	2154	319		19	9950	720
FI	9503513			Α		1996	0123	FI	1995-	3513			19	9950	720
NO	9502891			Α		1996	0123	NO	1995-	2891			19	9950	720
CN	.1116624			Α		1996	0214	CN	1995-	1096	18		19	950'	720

JP 08053440	· А	19960227	JP 1995-183923	19950720
IL 114684	Α	19990620	IL 1995-114684	19950720
AT 205842	T	20011015	AT 1995-305085	19950720
ES 2160668	T3	20011116	ES 1995-305085	19950720
PT 693488	T	20020228	PT 1995-305085	19950720
BR 9503408	A	19960227	BR 1995-3408	19950721
US 5512684	Α	19960430	US 1995-512724	19950808
PRIORITY APPLN. INFO.:			US 1994-279456	A 19940722
			US 1995-422294	Al 19950414

OTHER SOURCE(S):

CASREACT 124:289249; MARPAT 124:289249

GΙ

A process for prepg. 6-alkoxy-3-(4-alkoxyphenyl)benzo[b]thiophenes (I; A = H; AB R = same or different C1-6 alkyl) in good yield on a manufacturing scale without generating a thick, potentially yield-reducing, paste and thereby without mixing problems, involves intramol. cyclization of  $\alpha$ -(3alkoxyphenylthio) -4-alkoxyacetophenones (II; R = same as above). invention also provides methods for converting  $\alpha$ -(alkoxyphenylthio)-4alkoxyacetophenones I (A = H; R = same as above) into 6-hydroxy-2-(4hydroxyphenyl) -3-[4-(2- aminoethoxy)benzoyl]benzo[B]thiophenes I (A = Q, R = H; R5 = NR1R2; wherein R1, R2 = C1-4 alkyl, or R1R2 = C4-6 polymethylene or CH2CH2OCH2CH2) via acylation of a dialkoxy benzo[b] thiophene I (A = H; R = same as above) with an acylating agent R4-Q (R4 = Cl, Br, an active ester, etc.; R5 = same as above) under Friedel-Crafts conditions. Thus, 164 g  $\alpha$ bromo-4-methoxyacetophenone was added portion-wise to a mixture of 100 g 4methoxybenzenethiol and 39 g KOH in 300 mL and denatured EtOH in a cooling and stirred for 10 min in the cooling bath and at ambient temperature for 3 h to give, after workup, 158 g  $\alpha$ -(3-methoxyphenylthio)-4- methoxyacetophenone. The latter compound (6.92 g) was added steadily over 1/2 h to a mixture of 41.5 g polyphosphoric acid and 13.8 g phosphoric acid and the reaction mixture was heated at 85° for 1.75 h and cooled to 50°, to give , after extraction with toluene and crystallization, the desired 6-isomer, I (A = H, R = Me) (69% yield). The latter compound (30 g) was heated with 90 g pyridine hydrochloride with stirring at 210° for 30 min to give, after workup, 25.5 g I (A = R = H), which (40 g) was acetylated by Ac2O in the presence of 4dimethylaminopyridine in pyridine to give 52.5 g I (A = H, R = Ac). This compound (20 g) was added to a solution of 4-(2-piperidinoethoxy) benzoyl chloride (prepared from 16.3 g of the benzoic acid derivative) in ClCH2CH2Cl and stirred vigorously, followed by adding 73.4 g AlCl3 over 3 min, and the resulting mixture was stirred for 1 h to give, after workup, the desired product I [A = Q (wherein R5 = piperidino), R = Ac] as an oil, which was saponified with a mixture of 275 mL MeOH and 55 mL 5 n aqueous NaOH under reflux to give 10.5 g the title compound I [A = Q, wherein R5 = piperidino, R = H].

ANSWER 30 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN Ь3

ACCESSION NUMBER: 1996:150242 CAPLUS Full-text

DOCUMENT NUMBER:

124:202950

TITLE:

Preparation of benzothiophene glucopyranosides as

antihyperlipidemics.

INVENTOR(S):

Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom,

APPLICATION NO.

DATE

Terry Donald; Lugar, Charles Willis Iii; Staten,

Gilbert Stanley

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 20 pp.

DATE

SOURCE: CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

KIND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

PAIBNI NO.	KIND DAIL	million no.	· ·
EP 683170	A1 19951122	EP 1995-303265	19950516
EP 683170	B1 19990922		
		GB, GR, IE, IT, LI, LU,	NI. PT SE
US 5567820		US 1995-404701	
		US 1995-405555	
ZA 9503975	A 19961118		19950516
AT 184880	T 19991015 T3 19991201		
			19950516
AU 9520121	A 19951130	AU 1995-20121	19950517
AU 683734			
JP 07316180	A 19951205	JP 1995-118338	19950517
FI 9502420	A 19951121	FI 1995-2420	19950518
NO 9501954	A 19951121	NO 1995-1954	19950518
NO 304686	B1 19990201		
CN 1116626	A 19960214	CN 1995-106322	19950518
CN 1039013	B 19980708		
BR 9502079	A 19960305	BR 1995-2079	19950518
HU 73788	A2 19960930	HU 1995-1466	19950518
	B 20010328		
IL 113780	A 19990620		19950518
GR 3032142	T3 20000427		
US 2004167080	A1 20040826		
PRIORITY APPLN. INFO.:	AT 20040020	US 1994-246655	
PRIORITI APPLIN. INFO.:			
		US 1995-405555	A1 19950315

OTHER SOURCE(S):

CASREACT 124:202950

GI

AB Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-0-tetraacetyl-D-glucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

L3 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:123714 CAPLUS Full-text

DOCUMENT NUMBER:

124:155994

TITLE:

Pharmaceutical compositions containing

2-phenyl-3-aryoylbenzothiophenes for for inhibiting

Ι

bone loss and lowering serum cholesterol

INVENTOR(S):

Draper, Michael W.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Can. Pat. Appl., 31 pp.

CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141999	A1	19950903	CA 1995-2141999	19950207
US 5478847	A	19951226	US 1994-205012	19940302
ZA 9500976 '	Α	19960807	ZA 1995-976	19950207
NZ 314699	A	20000728	NZ 1995-314699	19950207
EP 674903	A1	19951004	EP 1995-300842	19950210
R: AT, BE, CH,	DE, DK	, ES, FR, G	BB, GR, IE, IT, LI, LU,	NL, PT, SE
NO 9500774	A	19950904	NO 1995-774	19950228
RU 2100024	C1	19971227	RU 1995-102778	19950228
RU 2150275	C1	20000610	RU 1996-119781	19950228
AU 9513551	Α	19950907	AU 1995-13551	19950301
AU 702575	B2	19990225		
JP 07267861	Α	19951017	JP 1995-41769	19950301
JP 2818384	B2	19981030		
BR 9500784	Α	19951024	BR 1995-784	19950301
CN 1119530	Α	19960403	CN 1995-100021	19950301

HU 72638	A2	19960528	HU	1995-634	•	19950301
JP 10291932	Α	19981104	JP	1998-107550		19950301
JP 10310525	Α	19981124	JP	1998-107549		19950301
US 5610168	A	19970311	US	1995-422289		19950414
US 5641790	A	19970624	US	1995-422417		19950414
US 5747510	Α	19980505	US	1997-788984		19970127
US 39050 ·	E1	20060328	US	2003-375274		20030227
PRIORITY APPLN. INFO.:		•	US	1994-205012	Α	19940302
			JP	1995-41769	A3	19950301
			US	1995-422417	A1	19950414

AB A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in postmenopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

L3 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1995:991025 CAPLUS Full-text

DOCUMENT NUMBER:

124:106673

TITLE:

Methods for lowering serum cholesterol

INVENTOR(S):

Black, Larry J.; Bryant, Henry U.; Cullinan, George

J.; Kauffman, Raymond F.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	A	19951107	US 1993-159159	19931130
TW 383306	В	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	À	19950615	ZA 1993-9427	19931215
SK 279271	В6	19980805	SK`1993-1421	19931215
IL 108042	Α	19980104	IL 1993-108042	19931216
CZ 283863	B6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628	·	
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	C	20050614	•	
NO 9304740	Α	19940623	NO 1993-4740	19931221
AU 9352578	A	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		
BR 9305182	Α	19940816	BR 1993-5182	19931221
JP 06234632	Α	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	A	19941026	CN 1993-121277	19931222
CN 1043608	В	19990616		
AT 233559	T	20030315	AT 1993-310438	19931222
ES 2193142	T3	20031101	ES 1993-310438	19931222
PRIORITY APPLN. INFO.:	•	•	US 1992-995222	B2 19921222

$$\begin{array}{c|c} & \text{CO} & \text{OCH}_2\text{CH}_2\text{(CH}_2\text{)}_n\text{R}^2 \\ \\ \text{R}^1 & \text{S} & \text{CO} & \text{CO} \end{array}$$

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof. The tested compds. lowered LDL without significantly affecting primary sex targets.

L3 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1995:362913 CAPLUS Full-text

DOCUMENT NUMBER:

122:213884

TITLE:

A chemical probe for the estrogen receptor: synthesis

of the 3H-isotopomer of raloxifene

AUTHOR (S):

Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C.

David

CORPORATE SOURCE:

Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

SOURCE:

Journal of Labelled Compounds & Radiopharmaceuticals

(1995), 36(1), 43-9

CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER:
DOCUMENT TYPE:

Wiley Journal

LANGUAGE:

English

AB Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1-piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L3 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1994:700754 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER:

121:300754

TITLE:

[[(Alkylsulfonyl)oxy]benzo[b]thienyl]methanones and

[[(aminocarbonyl)oxy]benzo[b]thienyl]methanones

pharmaceuticals

INVENTOR (S):

Black, Larry John; Bryant, Henry Uhlman; Cullinan,

George Joseph

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 617030 EP 617030	A1 B1	19940928 19990526	EP 1994-301871	19940316
			BB, GR, IE, IT, LI, LU,	NL. PT. SE
	A		US 1993-35121	
	A	19950914		
CA 2119091		19940920		
NO 9400940		19940920		
		19940920		19940316
AU 9457863			AU 1994-57863	19940316
AU 670177		19960704	DD 1004 1103	10040316
BR 9401183		19941101		
HU 70549	A2	19951030		
AT 180479		19990615	AT 1994-301871	
ES 2132339	T3	19990816	ES 1994-301871	19940316
FI 9401262	Α	19940920	FI 1994-1262	19940317
JP 06321937	A	19941122	JP 1994-47091	19940317
CN 1097420	A	19950118	CN 1994-102910	19940317
US 5994371	A	19991130	US 1995-392445	19950222
US 5599833	A	19970204	US 1996-588670	19960117
US 5605924	A	19970225	US 1996-588663	19960117
US 5798351	A	19980825	US 1997-958535	19971027
PRIORITY APPLN. INFO.:			US 1993-35121	
				A3 19950222
OTHER SOURCE(S):	MARPAT	121:300754		

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G1

# \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The (4-alkoxybenzoyl)benzo[b]thiophene-6-sulfonates and (4-alkoxybenzoyl)benzo[b]thien-6-yl carbamates I (R = OH, alkoxysulfonyl, carbamoyl; R1 = H, OH, halo, etc.; R2 = pyrrolidino, piperidino, etc.; X = bond, methine) were disclosed as agents for inhibiting the loss of bone, lowering serum cholesterol levels and therapeutically treating hormone dependent mammalian breast and uterine carcinoma. A specifically claimed example compound is [6-[(pentylsulfonyl)oxy]-2-[4-[(pentylsulfonyl)oxy]phenyl]benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone (II).

L3 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1984:448784 CAPLUS Full-text

DOCUMENT NUMBER:

1984:448784 CAPLOS FUII-CEX

TITLE:

Antiestrogens. 2. Structure-activity studies in a series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic

estrogenicity

AUTHOR(S):

Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.;

Peters, Mary K.; Black, Larry J.; Thompson, Allen R.;

Falcone, Julie F.; Clemens, James A.

Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, CORPORATE SOURCE:

46285, USA

Journal of Medicinal Chemistry (1984), 27(8), 1057-66 SOURCE:

CODEN: JMCMAR; ISSN: 0022-2623

Ι

DOCUMENT TYPE:

Journal

LANGUAGE:

GI

English

In an effort to prep. nonsteroidal antiestrogens demonstrating greater AB antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

CAPLUS COPYRIGHT 2007 ACS on STN ANSWER 36 OF 38

ACCESSION NUMBER:

1984:156501 CAPLUS Full-text

DOCUMENT NUMBER:

100:156501

TITLE:

Antiestrogenic and antiandrogenic benzothiophenes

INVENTOR(S): Jones, Charles D.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	AP	PLICATION NO.		DATE
					-	
US 4418068	Α	19831129	US	1981-331042		19811216
ZA 8202247	Α	19831130	ZA	1982-2247		19820401
PRIORITY APPLN. INFO.:			US	1981-246335	A2	19810403
OTHER SOURCE(S):	CASREA	CT 100:15650	1			
GI		•				

Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es AB I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un) substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2piperidinoethoxy)benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03 µg estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

CAPLUS COPYRIGHT 2007 ACS on STN ANSWER 37 OF 38

1983:71917 CAPLUS Full-text ACCESSION NUMBER:

98:71917 DOCUMENT NUMBER:

TITLE: Benzothiophene compounds

INVENTOR(S): Jones, Charles David

PATENT ASSIGNEE(S): Eli Lilly and Co., USA SOURCE: Eur. Pat. Appl., 107 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT	NO.	KIN	ID DATE	AI	PLICATION	NO.	DATE
EP 625	03	A)	1982	1013 E	1982-301	737	19820401
R	BE, CH,	DE, FR,	GB, IT,	LÜ, NL, S	SE		
AU 828	12265	Α	1982	1007 AU	J 1982-822	65	19820401
AU 559	658	В2	1986	1002			
GB 209	7788	Α	1982	1110 GF	3 1982-968	0	19820401
GB 209	7788	В	1985	0424			
JP 57	81081	·A	1982	1108 J	1982-564	79	19820402
PRIORITY A	PLN. INFO	).:		US	1981-246	335 A	19810403
				US	1981-331	045 A	19811216

[(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were AB prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

L3 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1983:71916 CAPLUS Full-text

DOCUMENT NUMBER:

98:71916

TITLE:

3-(4-Aminoethoxybenzoyl)benzo[b]thiophenes

Jones, Charles David; Goettel, Mary Elizabeth

INVENTOR(S): PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 59 pp.

CODEN: EPXXDW .

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PA	TENT NO.			KINI		DATE	AP	PLICATION NO.		DATE
	62504 62504			A1 B1		19821013 19860102	EP	1982-301738		19820401
	R: AT,	BE,	CH,	DE,	FR	, GB, IT,	LU, N	L, SE		
US	4358593			Α		19821109	US	1981-246334		19810403
IL	65378			Α		19860228	IL	1982-65378		19820330
CA	1167037			A1		19840508	CA	1982-400300	•	19820331
GB	2097392			Α		19821103	GB	1982-9679		19820401
GB	2097392			В		19850424				
DD	201793	•		<b>A</b> 5		19830810	DD	1982-238654		19820401
CS	227348			B2		19840416	CS	1982-2357		19820401
PL	130867			B1		19840929	PL	1982-235752		19820401
AT	17243			$\mathbf{T}$		19860115	AT	1982-301738		19820401
DK	8201512			Α		19821004	DK	1982-1512		19820402
FI	8201160			Α		19821004	FI	1982-1160		19820402
JP	57183788			Α		19821112	JP	1982-56480		19820402
ES	511124			A1		19830616	ES	1982-511124		19820402
HU	28787			A2		19831228	HU	1982-1026		19820402
HU	191353			B		19870227				
SU	1155157			<b>A3</b>		19850507	SU	1982-3417550		19820402

PRIORITY APPLN. INFO .:

US 1981-246334 A 19810403 US 1981-246335 A 19810403 US 1981-331045 A 19811216 EP 1982-301738 A 19820401

OTHER SOURCE(S):

MARPAT 98:71916

Benzothiophenes I [R = H; R1 = COC6H4O(CH2)2NR2R3-4; R2 = R3 = alkyl; R2R3 = (CH2)4-6, (CH2)2O(CH2)2, etc.] were prepared by Friedel-Crafts acylation of I (R = Ac, Bz, MeSO2; R1 = H) followed by hydrolysis of the ester groups. Thus, HSC6H4OMe-3 was treated with BrCH2COC6H4OMe-4 to give 3-MeOC6H4SCH2COC6H4OMe-4, which was cyclized with polyphosphoric acid to give I (R = Me, R1 = H). Demethylation of the latter followed by esterification with MeSO2Cl gave I (R = MeSO2, R1 = H; II). Friedel-Crafts acylation of 4 g II with 4-Me2N(CH2)2OC6H4COCl gave 6.2 g I [R = MeSO2, R1 = COC6H4O(CH2)2NMe2-4, III]. Hydrolysis of III gave I (R = H). I are estrogens, antiestrogens, and antiandrogens (no data).

=> file req COST IN U.S. DOLLARS SINCE FILE TOTAL **ENTRY** SESSION FULL ESTIMATED COST 115.67 124.13 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION -30.42 CA SUBSCRIBER PRICE -30.42

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## http://www.cas.org/support/stngen/stndoc/properties.html

piperidinyl)ethoxy]phenyl]-, hydrochloride (9CI)

CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl] [4-[2-(1-piperidinyl)ethoxy]phenyl]-, hydrochloride (1:1) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-

OTHER NAMES:

CN Bonebay

CN Bontact

CN Evista

CN Fiona

CN Keoxifene hydrochloride

CN LY 156758

CN Ralofen

CN Raloxifene hydrochloride

CN Reloxafine

MF C28 H27 N O4 S . Cl H

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, EMBASE, HSDB\*, IMSPATENTS, IMSRESEARCH, IPA, MRCK\*, MSDS-OHS, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL (\*File contains numerically searchable property data)

CRN (84449-90-1)

● HCl

#### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

329 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
329 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 8.25 132.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -30.42

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FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9 FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

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### http://www.cas.org/infopolicy.html

=> s 14

L5 329 L4

=> d scan

L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN

CC 63-6 (Pharmaceuticals)

TI Preparation of raloxifene hydrochloride capsules and establishment of its quality control standard

ST raloxifene hydrochloride capsules dissoln quality control

IT Drug delivery systems

(capsules; preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

IT Dissolution

Quality control

(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

IT 63-42-3, Lactose 9004-32-4, Carboxymethyl cellulose sodium 9004-34-6, Cellulose, biological studies

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

IT 82640-04-8, Raloxifene hydrochloride

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)

(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

### HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

- L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
- CC 2-4 (Mammalian Hormones)

Section cross-reference(s): 1

- TI Effectiveness of combined GnRH analogue plus raloxifene administration in the treatment of uterine leiomyomas: a prospective, randomized, single-blind, placebo-controlled clinical trial
- ST leuprolide acetate SERM raloxifene pelvic pain menorrhagia uterine leiomyomas
- IT Human

(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Intestine, disease

(constipation; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Menopause

(hot flash; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Uterus, neoplasm

(leiomyoma; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Menstrual disorder

(menorrhagia; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Body, anatomical

(pelvis, pain; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Menopause

(premenopause; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Estrogen receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective modulator of; GnRH analog (Enantone) plus raloxifene
hydrochloride (Evista) effectiveness in treatment of premenopausal
women with uterine leiomyomas)

IT Urinary system, disease

(urinary frequency; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT 74381-53-6, Leuprolide acetate

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Enantone; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

82640-04-8, Raloxifene hydrochloride RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

#### HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 CAPLUS COPYRIGHT 2007 ACS on STN 329 ANSWERS L5 IC ICM C07D333-64 ICS C07D333-56 27-9 (Heterocyclic Compounds (One Hetero Atom)) CC TT Demethylation process for preparing benzo[b]thiophenes demethylation benzothiophene benzenethiol ST 63675-73-0P 63675-74-1P 84541-36-6P IT RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (demethylation process for preparing benzo[b]thiophenes) 63676-25-5P **82640-04-8P** 84449-87-6P IT 84449-90-1P 215662-11-6P 215662-12-7P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation) (demethylation process for preparing benzo[b]thiophenes) 108-90-7, Chlorobenzene, uses TT RL: NUU (Other use, unclassified); USES (Uses) (demethylation process for preparing benzo[b]thiophenes) 2632-13-5 7340-90-1 7446-70-0, Aluminum chloride, reactions IT 15570-12-4, 3-Methoxybenzenethiol 84449-80-9 RL: RCT (Reactant); RACT (Reactant or reagent) (demethylation process for preparing benzo[b]thiophenes) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 CAPLUS COPYRIGHT 2007 ACS on STN L5 329 ANSWERS IC ICM A61K031-445 ICS A61K031-40; A61K031-38 INCL 514324000 63-6 (Pharmaceuticals) Section cross-reference(s): 1 TI Methods of decreasing serum calcium levels benzoyl benzothiophene calcium blood decrease; raloxifene calcium blood ŚТ decrease 82640-04-8, Raloxifene hydrochloride 84449-90-1, Raloxifene IT RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (benzoylbenzothiophene derivs. for decreasing serum calcium levels) 7440-70-2, Calcium, biological studies IT RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (benzoylbenzothiophene derivs. for decreasing serum calcium levels) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 CAPLUS COPYRIGHT 2007 ACS on STN L5 329 ANSWERS IC C12Q001-02 INCL 435029000 2-1 (Mammalian Hormones) CC Cell culture for screening estrogen agonists and antagonists TI estrogen agonist screening cell culture; antagonist estrogen screening ST

cell culture . Animal cell line

IT

```
(C7 MCF7-173, in screening of estrogen agonists/antagonists)
IT
     Estrogens
     RL: ANST (Analytical study)
        (agonists, cell culture method for screening of)
     Cell proliferation
IT
        (cells dependent on estrogens for, in screening of estrogen
        agonists/antagonists)
IT
     Charcoal
     RL: ANST (Analytical study)
        (dextran-, human serum stripped with, for maintaining medium in cell
        culture method for screening of estrogen agonists/antagonists)
     Blood serum
TΤ
        (fetal bovine, for maintaining medium in cell culture method for
        screening of estrogen agonists/antagonists)
IT
     Animal tissue culture
        (for estrogen agonist/antagonist screening)
IT
     Proteins, biological studies
     RL: BIOL (Biological study)
        (inhibitory to proliferation of estrogen-dependent cells in vitro, for
        cell culture method for screeing of estrogen agonists/antagonists)
IT
     Estrogens
     RL: PRP (Properties)
        (antiestrogens, cell culture method for screening of)
TT
     Mammary gland
        (neoplasm, cells of, in screening of estrogen agonists/antagonists)
IT
     50-27-1, Estriol 50-28-2, Estradiol, biological studies 53-16-7,
     Estrone, biological studies
     RL: ANST (Analytical study)
        (agonists and antagonists of, cell culture method for screening of)
     9004-54-0, Dextran, biological studies
IT
     RL: BIOL (Biological study)
        (charcoal-, human serum stripped with, for maintaining medium in cell
        culture method for screening of estrogen agonists/antagonists)
     10540-29-1, Tamoxifen
                             34816-55-2, Moxestrol
                                                      63676-25-5, LY117018
     71794-60-0, 11β-Chloromethylestradiol 82640-04-8, LY156758
     120382-04-9, RU39411
                           57-83-0, Progesterone, biological studies
     RL: ANST (Analytical study)
        (estrogen agonist/antagonist activity of, determination of, cell culture
method
        for)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0
=> s 14/prep
           329 L4
       4449106 PREP/RL
            34 L4/PREP
                 (L4 (L) PREP/RL)
=> d 16 ibib abs 1-
YOU HAVE REQUESTED DATA FROM 34 ANSWERS - CONTINUE? Y/(N):y
     ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN
L6
                         2007:265820 CAPLUS Full-text
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         146:448285
TITLE:
                         Benzothiophenes, formulations containing same, and
                         methods
                         Cullinan, George J.; Palkowitz, Alan D.
INVENTOR(S):
PATENT ASSIGNEE(S):
                         USA
```

Hung. Pat. Appl., 40pp.

SOURCE:

CODEN: HUXXCV

DOCUMENT TYPE:

Patent Hungarian

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	HU 9901882	A2	20000228	HU 1999-1882	19970219
	HU 9901882	A3	20000328		
]	PRIORITY APPLN. INFO.:			HU 1999-1882	19970219
(	OTHER SOURCE(S):	MARPAT	146:448285		
(	3I				

Ι

$$\begin{array}{c|c} x & & OCH_2CH_2 \stackrel{0}{N} - R^3 \\ \hline R^2 & & R^2 \end{array}$$

AB Benzothiophene N-oxides I [R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6hydroxybenzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

CAPLUS COPYRIGHT 2007 ACS on STN L6 ANSWER 2 OF 34

ACCESSION NUMBER:

2006:958171 CAPLUS Full-text

DOCUMENT NUMBER:

147:9760

TITLE:

Synthesis of raloxifene hydrochloride

AUTHOR(S):

Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong,

CORPORATE SOURCE:

Ping

Shenyang Institute of Chemical Technology, Faculty of Pharmaceutical-Engineering, Shenyang, 110142, Peop.

Rep. China

SOURCE:

Zhongguo Xinyao Zazhi (2005), 14(7), 882-884

CODEN: ZXZHA6; ISSN: 1003-3734

PUBLISHER:

Zhongguo Xinyao Zazhi Youxian Gongsi

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps,

including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:1257978 CAPLUS Full-text

DOCUMENT NUMBER:

144:135192

TITLE:

Manufacture of raloxifene-hydrochloride-containing medicines for treating bone fracture delayed union or

nonunion.

INVENTOR(S):

Zhang, Jianhao; Huang, Haibo

PATENT ASSIGNEE(S):

Peop. Rep. China

SOURCE:

Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp.

CODEN: CNXXEV

DOCUMENT TYPE:

Patent

LANGUAGE:

Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1615860	A	20050518	CN 2003-10113253	20031111
PRIORITY APPLN. INFO.:			CN 2003-10113253	20031111

The title medicines are manufd. from (by wt.) raloxifene hydrochloride (35-AB 45%) as effective components, diluent (50-60%), disintegrant (2-4%), lubricant (0.5-1%), and adhesive (2-3%). The medicines can be produced into various drug forms such as tablets, capsules, suspensions, powders, granules, solns., etc., and have advantages of short course of treatment, high recovery rate, etc.

L6 ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:547361 CAPLUS Full-text

DOCUMENT NUMBER:

143:59836

TITLE:

A process for preparing benzoic acid derivatives,

useful as intermediates for preparation of raloxifene

INVENTOR(S):

Luke, Wayne Douglas

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005137396	A1	20050623	US 2003-745188	20031222
US 7012153	· B2	20060314		
RIORITY APPLN. INFO.:			US 2003-745188	20031222

CASREACT 143:59836; MARPAT 143:59836 OTHER SOURCE(S):

The invention relates to a prepn. of benzoic acid derivs. of formula RO2C-p-C6H4-O(CH2)2-3N(R1)R2 [wherein: R is alkyl; R1 and R2 are independently alkyl, or combined together with the nitrogen atom form piperidinyl, pyrrolidinyl, or morpholinyl, etc.], useful as intermediates for preparation of raloxifene. For instance, 4-[2-(piperidin-1- yl)ethoxy]benzoic acid hydrochloride was prepared via etherification of Me 4-hydroxybenzoate by  $1-(\beta$ - chloroethyl)piperidine hydrochloride and subsequet hydrolysis with a yield of 99.2%.

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN L6 ACCESSION NUMBER: 2005:29327 CAPLUS Full-text

9

DOCUMENT NUMBER:

142:134465

TITLE:

Process for preparing raloxifene hydrochloride

INVENTOR(S):

Ferrari, Massimo; Zinetti, Fabrizio; Belotti, Paolo

PATENT ASSIGNEE(S):

Erregierre S.p.A., Italy

SOURCE:

PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA:	rent 1	NO.			KIN	D									D	ATE	
							-							-				
	WO	2005	0031	16		A1		20050113		WO 2004-EP51263				20040628				
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜŻ,	NA,	NI,
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
		RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
			ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
			SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,
			SN,	TD,	TG													
	CA	2549	354			A1		2005	0113	(	CA 2	004-3	2549	354		2	040	628
	EP	1641	773			<b>A1</b>		2006	0405	1	EP 2	004-	7419	07		2	040	628
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	FI,	RO,	CY,	TR,	BG,	CZ,	EE,	HU,	PL,	SK				•
	US	2007	10014	47		A1		2007	0503	1	US 2	005-	5627	62 .		2	0051	227
PRIO	RITY	APP	LN.	INFO	. :						IT 2	003-1	MI13:	33	ž	A 2	0030	630
														263			0040	628

OTHER SOURCE(S): CASREACT 142:134465

A process for prepg. raloxifene hydrochloride with a purity greater than 98% AR and low aluminum content comprises the following stages : (a) demethylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene in pyridine and hydrochloric acid to obtain 6-hydroxy-2-(4- hydroxyphenyl)benzo[b]thiophene in pyridine hydrochloride, (b) acetylation of 6-hydroxy-2-(4hydroxyphonyl)benzo[b]thiophene with an acetylating agent to obtain the corresponding 6-acetoxy-2-(4- acetoxyphenyl)benzo[b]thiophene (I), (c) acylation of 6-acetoxy-2-(4- acetoxyphonyl)benzo[b]thiophene with 4-(2piperidinoethoxy) benzoylchloride hydrochloride with aluminum trichloride in a halogenated solvent to obtain 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2piperidinoethoxy)benzoyl] - benzo[b]thiophene, (d) hydrolysis of 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene according to the following operating conditions: (d1) treatment of 6-acetoxy-2-(4-acetoxyphonyl)-3-[4- (2-piperidinoethoxy)benzoyl]benzo[b]thiophene with alkaline hydroxide in alc. solvent, (d2) acidification of the product obtained in the preceding stage (d1) with a strong acid, to obtain the corresponding raloxifene salt with the strong acid, characterized in that the strong acid used in stage (d2) is concentrated hydrochloric acid. Thus, thionyl chloride was added to a mixture of 4-(2-piperidinoethoxy) benzoic acid HCl salt and pyridine in refluxing methylene chloride; the mixture was stirred for 1 h and

the solvent was distilled off; the mixture was cooled to 20°C, and I was added. The resulting mixture was mixed with aluminum trichloride in methylene chloride at 15°C to 30°C; the mixture was stirred for 1 h and was worked up: the product was treated with sodium hydroxide in methanol; water, Et acetate, and HCl were added; the suspension was centrifuged to give crude raloxifene hydrochloride.

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2004:617920 CAPLUS Full-text

DOCUMENT NUMBER:

CORPORATE SOURCE:

142:463529

TITLE:

Synthesis of raloxifene hydrochloride Gong, Ping; Zhao, Yanfang; Wang, Dun

AUTHOR(S):

School of Pharmaceutical Engineering, Shenyang

Pharmaceutical University, Shenyang, 110016, Peop.

Rep. China

SOURCE:

Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113

CODEN: SYDXFF; ISSN: 1006-2858

PUBLISHER:

Shenyang Yaoke Daxue Xuebao Bianjibu

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

OTHER SOURCE(S):

CASREACT 142:463529

AB Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-

hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3,

saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR,

13C NMR.

L6 ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2002:348716 CAPLUS Full-text

DOCUMENT NUMBER:

138:137104

TITLE:

Synthesis of Raloxifene hydrochloride as selective

estrogen receptor modulator

AUTHOR (S):

Chen, Yanzhong; Liu, Yingxiang

CORPORATE SOURCE:

Guangdong College of Pharmacy, Canton, 510224, Peop.

Rep. China

SOURCE:

Guangdong Yaoxueyuan Xuebao (2002), 18(1), 1-3, 20

CODEN: GYXUF8

PUBLISHER:

Guangdong Yaoxueyuan

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

OTHER SOURCE(S):

CASREACT 138:137104

AB Raloxifene was synthesized from α-bromo-p-methoxyacetophenone and m-methoxybenzenethiol via condensation, cyclization, acylation, and demethylation with the overall yield 49.2%. The chemical structure of compound was confirmed by 1H NMR, MS, IR, and elementary anal. The reaction conditions were mild and starting materials were com. available.

L6 ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2001:247325 CAPLUS Full-text

DOCUMENT NUMBER:

134:266100

TITLE:

Synthesis of 4-[(2-piperidin-1-yl)ethoxy]benzoic acid

for manufacture of Raloxifene hydrochloride

INVENTOR (S):

Luke, Wayne Douglas

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE:

PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.			KIN	D	DATE		i	APPL	ICAT:	ION 1	NO.		D.	ATE	
					-									-		
WO 200	10233	69		A2		2001	0405	1	WO 2	000-1	JS21	974		2	0000	918
· W:	AE,															
	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,
•	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,
	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,
	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	.UG,	US,	ŲΖ,	VN,
	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM				
RV	: GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	ΒĒ,	CH,	CY,
	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,
	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
EP 122	0847			A2		2002	0710	1	EP 2	000-	9666	91		2	0000	918
R	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
	IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL							
JP 200	35103	13		T		2003	0318		JP 2	001-	52652	22		2	0000	918,
PRIORITY A	PLN.	INFO	.:					1	US 1	999-	15620	05P	]	P 1	9990	927
•								1	WO 2	000-1	JS21	974	7	W 2	0000	918
OMITTED COLLEGE	m / a) .			(1) (1)	222	12	1.26	C100	. M7.	שעמם	124	. 266	100			

OTHER SOURCE(S): CASREACT 134:266100; MARPAT 134:266100

AB An improved process for the prepn. of 4[(2-piperidin-1-yl)ethoxy]benzoic acid derivs. comprises reacting haloalkyl amine X(CH2)nNR1R2 (X = halogen; R1, R2 = C1-4 alkyl, combined with nitrogen atom to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, 1-hexamethyleneimino group; n = 2, 3) with C1-6 alkyl p-hydroxybenzoate in the presence of a hydrated inorg. base in an appropriate solvent.

L6 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1999:12339 CAPLUS Full-text

DOCUMENT NUMBER:

130:66385

TITLE:

Process for preparing benzoic acid derivatives as intermediates in the synthesis of benzothiophenes

INVENTOR(S):

Chelius, Erik Christopher

PATENT ASSIGNEE(S): SOURCE:

Eli Lilly and Company, USA U.S., 7 pp.

i.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

T: 2

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
				· <b>-</b>	
US 5852193	A	19981222	US 1998-69277		19980429
US 6075146	Α	20000613	US 1998-123889		19980728
PRIORITY APPLN. INFO.:			US 1997-45162P	P	19970430
		•	US 1998-69277	<b>A3</b>	19980429
OTHER SOURCE(S):	CASRE	ACT 130:66385	; MARPAT 130:66385		

### \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compds. [I; R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; R6 = carboxy protecting group] were prepared byreacting a hydroxylamine HO(CH2)nNR1R2 with a compound selected from W2O and W-halo (wherein W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.) followed by reaction of the resulting Y1(CH2)nNR1R2 (Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, etc.) with a compound II. Compds. I can be then reacted with benzothiophenes III (R4, R5 = hydroxy protecting groups) to afford compds. IV (R4, R5 = , H, hydroxy protecting groups) (example of such reaction was given).

REFERENCE COUNT: THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS 29 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

1.6 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:721690 CAPLUS Full-text

DOCUMENT NUMBER: 130:3769

Processes for preparing benzothiophenes TITLE:

INVENTOR(S): McGill, John McNeil, III; Misner, Jerry Wayne; Zhang,

Tony Yantao

PATENT ASSIGNEE(S): Eli Lilly and Co., USA PCT Int. Appl., 26 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PA	TENT :	NO.			KINI	)	DATE			APPI	LICAT	ON 1	NO.		D	ATE	
						-									-	- <b></b> -	
WO	9849	156			<b>A1</b>		1998:	1105		WO :	1998 <b>-</b> 1	JS850	9		1:	99804	128
	W:	AL,	AM,	AU,	ΑZ,	BA,	BB,	ВĠ,	BR,	BY	, CA,	CN,	CU,	CZ,	EE,	GE,	GH,
		GM,	GW,	HU,	ID,	IL,	IS,	JP,	ΚE,	KG,	, KP,	KR,	KZ,	LC,	LK,	LR,	LS,
		LT,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO	, NZ,	PL,	RO,	RU,	SD,	SG,	SI,
											, UZ,						
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW	, BF,	ВJ,	CF,	CG,	CI,	CM,	GA,
		GN,	ML,	MR,	NE,	SN,	TD,	TG									•
CA	2287	943			A1		1998	1105		CA :	1998-2	22879	943		. 19	99804	128
AU	9872	613			Α		1998:	1124		AU :	1998-1	72613	3		1:	99804	128
BR	9809	439			Α		20000	0613		BR :	1998-9	9439			1:	99804	128
HU	2000	0318	7		A2		2001	0528		HU 2	2000-3	3187			1:	99804	128
JP	2001	5223	72		T		2001	1113	1	JP :	1998-5	5472	77		19	99804	128
US	6090	949			Α		20000	0718	•	us :	1998-6	5949	7		1:	99804	129
EP	8755	10			A1		1998:	1104		EP :	1998-3	30331	74		1	99804	130
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	, IT,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FI,	RO							•			
MX	9909	883			Α		20000	0331	1	MX :	1999-9	9883			1:	99910	27
PRIORIT	Y APP	LN.	INFO	. :					1	US :	1997-4	1517	7 P	I	2 1	99704	130
									1	wo :	1998-U	JS85(	9	V	V 19	99804	128
OTHER S	OURCE	(s):			CASI	REAC	T 130	0:376	59;	MARI	PAT 13	30:37	769				

<sup>\*</sup> STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compds. [I; Y = Cl, Br, I, SO2(Cl-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = Cl-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:721501 CAPLUS Full-text

DOCUMENT NUMBER: 130:3768

TITLE: Demethylation process for preparing benzo[b]thiophenes

INVENTOR(S): Hoard, David Warren; Luke, Wayne Douglas

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: Eur. Pat. Appl., 13 pp. CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 875511	A1 19981104	EP 1998-303345	19980429
R: AT, BE, CH,	DE, DK, ES, FR, GB	, GR, IT, LI, LU, NL,	SE, MC, PT,
IE, SI, LT,	LV, FI, RO		
CA 2236254	A1 19981030	CA 1998-2236254	19980427
JP 11005789	A 19990112	JP 1998-118628	19980428
US 5994547	A 19991130	US 1998-69500	19980429
PRIORITY APPLN. INFO.:	•	US 1997-45156P	P 19970430
OTHER SOURCE(S):	CASREACT 130:3768;	MARPAT 130:3768	
GT .			

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

AB. The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be

carried out in the same reaction vessel without isolation of the acylated, protected material.

REFERENCE COUNT:

10

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1998:721498 CAPLUS Full-text

DOCUMENT NUMBER:

130:3767

TITLE:

Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceuticals

INVENTOR(S):
PATENT ASSIGNEE(S):

Chelius, Erik Christopher Eli Lilly and Company, USA

COIDCE.

Eur. Pat. Appl., 16 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

Engli

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 875507	A1	19981104	EP 1998-303340	19980429
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IT, LI, LU, 1	NL, SE, MC, PT,
IE, SI, LT,	LV, FI	, RO	·	
CA 2231013	A1	19981030	CA 1998-2231013	19980304
JP 10316674	Α	19981202	JP 1998-116564	19980427
PRIORITY APPLN. INFO.:			US 1997-45162P	P 19970430
OTHER SOURCE(S):	CASREA	CT 130:3767;	MARPAT 130:3767	•
GI				

The novel intermediates Y1(CH2)nNR1R2 [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, 2,2,2-trifluoroethylsulfonyloxy, trifluoroacetoxy], useful as intermediates in synthesis of benzothiophenes I and their salts, were prepared by reaction a hydroxylamine HO(CH2)nNR1R2 with W2O and W(halo) [W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.].

REFERENCE COUNT:

19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:719256 CAPLUS Full-text

DOCUMENT NUMBER:

130:3764

TITLE:

A regioselective alkylation process for preparing

substituted benzo[b]thiophenes

INVENTOR(S):

McGill, John McNeil, III; Miller, Randal Scot

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

PCT Int. Appl., 22 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT 1				APPLICATION NO.	DATE
WO 9848			19981105	WO 1998-US8477	19980428
₩:	AL, AM, AT,	AU, AZ,	BA, BB,	BG, BR, BY, CA, CH,	CN, CU, CZ, DE,
	DK, EE, ES,	FI, GB,	GE, GH,	GM, GW, HU, ID, IL,	IS, JP, KE, KG,
	KP, KR, KZ,	LC, LK,	LR, LS,	LT, LU, LV, MD, MG,	MK, MN, MW, MX,
				SE, SG, SI, SK, SL,	
	UA, UG, US,	UZ, VN,	YU, ZW,	AM, AZ, BY, KG, KZ,	MD, RU, TJ, TM
RW:			•	UG, ZW, AT, BE, CH,	
			•	MC, NL, PT, SE, BF,	
	CM, GA, GN,	ML, MR,	NE, SN,	TD, TG	
CA 2287	918	•	-	CA 1998-2287918	19980428
AU 9871	653	Α	19981124	AU 1998-71653	19980428
EP 9790'	75	A1	20000216	EP 1998-918798	19980428
R:	AT, BE, CH,	DE, DK.	ES. FR.	GB, GR, IT, LI, NL,	SE, PT, IE, FI
				JP 1998-547259	
				US 1998-69276	
PRIORITY APP		••		US 1997-45132P	
				WO 1998-US8477	
OTHER SOURCE	(S):	CASREAC	T 130:37	54; MARPAT 130:3764	23366126

$$\begin{array}{c} & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

The title benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, AΒ pyrrolidino, morpholino, etc.; n = 2, 3] such as raloxifene, were prepared by the regioselective alkylation of benzothiophene II with Y(CH2)nNR1R2 [Y = Cl, p-TsO] in the presence of a suitable base. 6

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS

#### RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:192131 CAPLUS Full-text

DOCUMENT NUMBER: 128:275070

TITLE: Benzothiophenes, formulations containing same, and

methods

INVENTOR(S): Cullinan, George Joseph; Palkowitz, Alan David

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 10 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	'			
US 5731342	Α	19980324	US 1997-787041	19970127
PRIORITY APPLN. INFO.:			US 1997-787041	19970127
OTHER SOURCE(S):	MARPAT	128:275070		
GI				

$$\begin{array}{c|c} X & & O \\ \hline & O \\ C \\ R \\ 1 \\ \hline & S \\ \end{array}$$

Benzothiophene N-oxides [I; R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:161136 CAPLUS Full-text

ACCESSION NUMBER: 1998:161136 CF DOCUMENT NUMBER: 128:221639

TITLE: Preparation of amorphous benzothiophenes for

pharmaceuticals

INVENTOR(S): Cuff, George W.; Thakkar, Arvind L.

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Cuff, George W.; Thakkar,

Arvind L.

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	ATENT NO. KIND DATE			APPLICATION NO.					DATE									
	WO	9808									wo	19	97-I	JS14	768.		1	9970	822
		W:	AL,	AM,	AU,	AZ,	BA,	BB,	BG,	BR,	BY	ζ, (	CA,	CN,	CU,	CZ,	EE,	GE,	GH,
			HU,	IL,	ÍS,	JΡ,	KE,	KG,	ΚP,	KR,	ΚZ	Ι, :	LC,	LK,	LR,	LT,	LV,	MD,	MG,
			MK,	MN,	MW,	MX,	NO,	NZ,	PL,	RO,	RU	J, 1	SD,	SG,	SI,	SK,	SL,	ТJ,	TM,
								UZ,											
		RW:	GH,	KE,	LS,	MW,	SD,	, SZ,	UG,	ZW,	BF	r', ]	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,
			ML,	MR,	NE,	SN,	TD,	, TG											
	EP	8266	82 .			<b>A1</b>		1998	0304		ΕP	19	97-3	30642	26		1	9970	822
	EP	8266	82																
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	٤, :	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			IE,	SI,	LT,	LV,	FI,	, RO											
	CA	2263	175			<b>A1</b>		1998	0305		CA	19	97-2	2263	175		1	9970	822
	AU	9742	335			Α		1998	0319		ĄU	19	97-4	1233	5		1	9970	822
	AU	7239	87																
,	IN	1829	40			<b>A1</b>		1999	0814		IN	19	97-0	CA15	19		1	9970	822
•	BR	9713	176			Α		2000	0208		BR	19	97-:	1317	5		1	9970	822
	CN	1244	124			Α		2000	0209		CN	19	97-3	1974	34		1	9970	822
	HU	2000	0117	2		A2		2001	0628	:	HÜ	20	00-3	1172				9970	
	HU	2000	0117	2		· A3		2002	0128										
	NZ	3338	39			Α		2001	0629	:	NZ	19	97-3	33383	39		1	9970	822
	IL	1286	41			Α		2001	1031		ΙL	19	97-3	12864	41		1	9970	822
		9900				T2		2002	0121		TR	19	99-4	103				9970	
	JP	2002	5141	74		T		2002	0514	1	JΡ	19	98-5	51174	44		1	9970	822
	ΑT	2342	95			T		2003	0315									9970	822
	ES	2195	0.89			Т3		2003	1201	:	ES	19	97-3	30642	26		1	9970	822
•	zA	9707	617			Α		1999	0225		ZA	19	97-	7617				9970	
	US	6713	494			B1		2004	0330	1	US	19	97-9	91874	11		1	9970	825
	NO	9900	914			Α		1999	0225		NO	19	99-9	914			1	9990:	225
	KR	2000	03594	41		Α		2000	0626	. :	KR	19	99-1	70168	32		1	9990:	227
PRIO	RITY	APP	LN.	INFO	. :	1				1	US	19	96-2	2483	lP	]	? 1	9960	828
																		9970	

OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT:

1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1997:640660 CAPLUS Full-text

DOCUMENT NUMBER: 127:307297

TITLE: Preparation of 3-[4-(2-aminoethoxy)benzoyl]-2-aryl-6-

hydroxybenzo[b]thiophenes.

INVENTOR(S): Jones, Charles David; McGill, John McNeill, III

PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Jones, Charles David; McGill,

John McNeill, III

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

						KIND DATE		APPLICATION NO.						DATE				
	9734									WO 1	996-1	US39:	34		1	9960:	320	
•	W:	AL,	AM,	AT,	AU,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,	ES,	
		FI,	GB,	GE,	HU,	IS,	JP,	KΕ,	KG,	KP,	KR,	KZ,	LK,	·LR,	LS,	LT,	LU,	
		LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	
		SI,	SK,	ТJ,	TM,	TR,	TT,	UA,	UG,	US,	UΖ,	VN,	AM,	AZ,	BY,	KG,	KZ,	
		MD,	RU,	ТJ,	TM													
	RW:	KE,	LS,	MW,	SD,	sż,	ŪĠ,	ΑT,	ВĒ,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	
											CF,							
		MR,	NE,	SN,	TD,	TG												
CA	2249	406			<b>A1</b>		1997	0925	(	CA 1	996-2	2249	406		1:	9960	320	
AU	9652	586 ·		•	Α		1997	1010		AU 1	996-	5258	6		1:	9960	320	
EP	8883	31			<b>A</b> 1		1999	0107	1	EP 1	996-	9088	92	·	1:	9960	320	
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	PT,	IE,	FI
JP	2000	5068	85		T		2000	0606		JP 1	997-	5334	24	•	1	9960	320	
ບຣ	6008	377			Α		1999	1228	1	JS 1	998-	12584	48		1:	9980	821	
PRIORIT	Y APP	LN.	INFO	.:		,			1	JS 1	996-:	13674	4 P	]	P 1:	9960	319	
	•								1	WO 1	996-1	JS39:	34	7	<b>v</b> 1:	9960	320	
OTHER S	OURCE	(s) :			CASI	REAC	T 12	7:30	7297	; MA	RPAT	127	:307	297				

Title compds. (I; R1 = H, OH; R2, R3 = alkyl; R2R3N = pyrrolidino, piperidino, hexamethyleneimino, morpholino; HX = HCl, HBr) were prepared by reaction of PhOCH2CH2NR2R3.HX (variables as above) with acyl derivative (II; R4 = H, alkoxy; R5 = alkyl; R6 = Cl, Br, OH) in the presence of BX3. Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene-3-carbonyl chloride (preparation given), and Ph 2-N-piperidinylethyl ether hydrochloride (preparation given) in 1,2-dichloroethane at 0° were treated with BCl3 in 1,2-dichloroethane at 0° followed by warming to 35° for 16-20 h to give 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride 1,2-dichloroethane solvate.

ANSWER 17 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN L6

ACCESSION NUMBER:

1997:124441 CAPLUS Full-text

DOCUMENT NUMBER:

126:143973

TITLE:

Diaryl vinyl sulfoxides, a process for their synthesis, and their use in the preparation of

benzothiophene derivatives

INVENTOR (S):

Aikins, James A.; Miller, Randal S.; Zhang, Tony Y. Eli Lilly and Co., USA; Aikins, James A.; Miller,

APPLICATION NO.

DATE

Randal S.; Zhang, Tony Y.

SOURCE:

PCT Int. Appl., 45 pp.

DATE

DOCUMENT TYPE:

Patent

CODEN: PIXXD2

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

KIND

PATENT NO.

PATENT ASSIGNEE(S):

PATENT INFORMATION:

															-		
WO											1996-					9960	
	W:	•	•	•	-				-		, CA,	-	-				
					-		-				KG,						
		LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX	, NO,	ΝŻ,	PL,	PT,	RO,	RU,	SD,
		•	SG														
	RW:	-	-				-				, DE,					GB,	GR,
											CF,					•	
US	5659	087			Α		1997	0819		US	1995-	4787	06		1	9950	
US	6372	945			В1		2002	0416		US	1995-	4831	30		1	9950	
_	2220										1996-						
AU	9660							•		AU	1996-	6092	0		1	9960	604
AU	6973	52			B2		1998	1001									
EP	8303	61			A1		1998	0325		ΕP	1996-	9182	11		1	9960	604
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	PT,	IE,
		SI,	LT,	LV,													
	1192										1996-					9960	
											1996-						
	1150						1999	0622		JP	1996-	5015	52		1	9960	604
HU	9900	922			.A2		1999	0728		HU	1999-	922			1	9960	604
HU	9900	922			A3		2000	0628									
NZ	3370	30					2000	1124			1996-					9960	
NZ	3370	31			Α		2001	0126		NZ	1996-	3370	31				
SG	1065	58		-8-	A1		2.004	1029		SG	1998-	4999			. 1	9960	604
NO	9705	578			Α						1997-				1	9971	203
NO	5987										2000-					0001	127
CN	1341	596			Α		2002	0327		CN	2000-	1307	79		2	0001	215
PRIORIT	Y APP	LN.	INFO	. :						US	1995-	4787	06	. 2			
							•				1995-					9950	
											1996-						
											1996-				W 1	9960	604
OTHER S	OURCE	(S):			CASI	REAC	T 12	6:143	3973	; M	ARPAT	126	:143	973			

GI

$$R^{1}$$
 $R^{2}$ 
 $R^{2$ 

The invention is directed to new diarylvinyl sulfoxides I [R1, R2 = H, alkoxy, AB arylalkoxy, halo, amino; R3 = thermally labile or acid-labile alkyl, alkenyl, or arylalkyl group], and to a new process for their synthesis. I are useful precursors for 2-aryl-substituted benzothiophenes II, which are in turn intermediates for the drugs III.HX [R1, R2 = H, halo, amino, OH; R4, R5 = alkyl; or NR4R5 = pyrrolidino, piperidino, hexamethyleneimino, morpholino; X = Cl, Br]. For instance, treatment of 4-MeOC6H4CH2COC6H4OMe-4 with TiCl4 in THF and reaction with Me3CSH and Et3N gave the vinyl sulfide (E)-4-MeOC6H4CH:C(SCMe3)C6H4OMe-4 [(E)-IV]. Alternatively, lithiation of 4-MeOC6H4CH2SCMe3 with BuLi and condensation with 4-MeOC6H4CHO gave (Z)-IV. Oxidation of either isomer of IV with a dilute AcOH solution of peracetic acid, in PhMe at -20°, gave the corresponding sulfoxide I [R1 = R2 = OMe; R3 = CMe3]. Dehydrative cyclization of, e.g., the (E)-sulfoxide, using p-MeC6H4SO3H catalyst under Dean-Stark conditions in PhMe, gave the benzothiophene II [R1 = R2 = OMe]. This was acylated by 4-(2piperidinoethoxy) benzoyl chloride HCl in the presence of BCl3 with concomitant demethylation to give the objective compound III.HCl [R1 = R2 = OH, NR4R5 = piperidino].

ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1997:113406 CAPLUS Full-text

DOCUMENT NUMBER:

126:117861

TITLE:

Process for the synthesis of benzo(b)thiophenes

Aikins, James A.; Zhang, Tony Y.

INVENTOR(S): PATENT ASSIGNEE(S):

Eli Lilly and Co., USA; Aikins, James A.; Zhang, Tony

Υ.

SOURCE:

PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT	NO.			KIN	D	DATE			APPL:	ICAT	ION 1	. O <i>n</i>		D	ATE	
					-									-		
WO 9640	676			A1		1996	1219		WO 1	996-1	US91	67		1	9960	604
W:	AL,	AM,	AT,	ΑU,	ΑZ,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,
	ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LK,	LR,	LS;

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LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
             SE, SG
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
                              19970225
                                            US 1995-484536
     US 5606076
                          Α
                                                                    19950607
                                             CA 1996-2223096
     CA 2223096
                          A1
                                19961219
                                                                    19960604
                                             AU 1996-60921
     AU 9660921
                                19961230
                                                                    19960604
     AU 702928
                          B2
                                19990311
     EP 859770
                                19980826
                                            EP 1996-918212
                          A1
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     EP 859770
                          B1
                                 19991208
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
             SI, LT, LV, FI
                                             CN 1996-195943
     CN 1192211
                                19980902
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     CN 1086699
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     BR 9609062
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                                            BR 1996-9062
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     JP 11506789
                          Т
                                19990615
                                             JP 1997-501555
                                                                    19960604
     HU 9900912
                          A2
                                19990728
                                            HU 1999-912
                                                                    19960604 .
     HU 9900912
                          A3
                                20000328
                          В
                                20010730
     HU 219735
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                                19991215
                                            AT 1996-918212
     AT 187450
                                                                    19960604
                          T3
                                            ES 1996-918212
     ES 2140859
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                                                                    19960604
                                            PT 1996-918212
     PT 859770
                          T
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                                                                    19960604
     IL 131440
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                                            IL 1996-131440
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                          Α
                                            NO 1997-5582
                                19971203
                                                                    19971203
     GR 3032666
                          Т3
                                20000630
                                            GR 2000-400364
                                                                    20000214
PRIORITY APPLN. INFO.:
                                            US 1995-484536
                                                                 A 19950607
                                             IL 1996-122378
                                                                 A3 19960604
                                            WO 1996-US9167
                                                                 W 19960604
OTHER SOURCE(S):
                         CASREACT 126:117861; MARPAT 126:117861
     The present invention is directed to a process for the synthesis of 2-
     arylbenzo[b]thiophenes. E.q., 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene
     was prepared from desoxyanisoin and 2-methyl-2-propanethiol via tert-Bu 4,4'-
     dimethoxystilbenyl sulfoxide.
L6
     ANSWER 19 OF 34
                      CAPLUS COPYRIGHT 2007 ACS on STN
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ACCESSION NUMBER:

1996:649600 CAPLUS Full-text

DOCUMENT NUMBER:

125:266032

TITLE:

Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal

syndrome-associated indications and estrogen-dependent

diseases, and pharmaceuticals containing them

INVENTOR(S):

Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729964	A1	19960904	EP 1996-300878	19960209
EP 729964	B1	20010509		
·R: AT, BE, CH,	DE, DK,	ES, FR, GB	, GR, IE, IT, LI, LU,	NL, PT, SE
US 6479517	В1	20021112	US 1995-395944	19950228
ES 2158242	T3	20010901	ES 1996-300878	19960209

CA 2169414	A1	19960829	CA	1996-2169414		19960213
JP 08259560	Α	19961008	JP	1996-25281		19960213
US 5998443	A	19991207	US	1997-946842		19971008
PRIORITY APPLN. INFO.:			US	1995-395944	Α	19950228
OTHER COURCE (C).	маррат	125.266032				

OTHER SOURCE(S): MARPAT 125:266032

GT

Phosphorus-contq. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(O-AB alkyl)2, OPO(0-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds. of the invention, as well as pharmaceutical compns. containing compds. of the invention.

ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN 1996:319150 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

125:86484

TITLE:

Preparation of vinyl sulfenic acid derivatives as

benzo[b] thiophene intermediates

INVENTOR (S):

Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 15 pp. CODEN: USXXAM

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND US 5512701 19960430 US 1995-482692 19950607 Α CA 2224225 Αl 19961219 CA 1996-2224225 19960604 WO 9640693 A1 19961219 WO 1996-US9460 19960604 AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,

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SE, SG
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM
                                            AU 1996-61003
                                                                   19960604
     AU 9661003
                          Α
                                19961230
     AU 698076
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                                19981022
     EP 830362
                          A1
                                19980325
                                            EP 1996-918314
                                                                   19960604
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
             SI, LT, LV, FI
                                19980902
                                            CN 1996-195947
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     CN 1192215
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     CN 1068883
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                                20010725
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                                            BR 1996-8847
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                                            JP 1997-501774
                                                                   19960604
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                                            HU 1999-923
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                                20010520
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                                            NO 1997-5633
                                                                   19971204
                          Α
     NO 9705633
                                            CN 2000-130796
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     CN 1330071
                          Α
                                            US 1995-482692
                                                                A 19950607
PRIORITY APPLN. INFO.:
                                            US 1995-483607
                                                                A 19950607
                                            WO 1996-US9460
                                                                W 19960604
OTHER SOURCE(S):
                         CASREACT 125:86484; MARPAT 125:86484
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4-R1C6H4CH:C(R9)C6H4R2-4 [I; R1,R2 = H, (ar)alkoxy, halo, NH2; R9 = SR4; R4 = OSi(R)3, NR5R6, SR8; R = (ar)alkyl, aryl; R5,R6 = H, (ar)alkyl; NR5R6 = pyrrolidino, piperidino, etc.; R8 = (ar)alkyl, aryl] were prepared by treating I [R9 = SOR3; R3 = labile alk(en)yl or aryl] with a silylating agent optionally followed by reaction with HNR5R6 or HSR8. Thus, (E)-I (R1 = R2 = OMe)(II; R9 = SOCMe3)(preparation given) was treated with (Me2CSiNH)2CO in PhMe followed by Me2NH, in the same pot, to give I (R1 = R2 = OMe, R9 = SNMe2) as a mixture of (E)- and (Z)-isomers. The latter mixt was treated with TsOH to give 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophe ne.

L6 ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1996:307324 CAPLUS Full-text

DOCUMENT NUMBER:

124:343103

TITLE:

Preparation of unsolvated crystalline 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2piperidinoethoxy)benzoyl]benzo[b]thiophene

hydrochloride.

INVENTOR(S):

Smith Labell, Elizabeth; Luke, Wayne Douglas; McNeill

McGill, John, III; Miller, Randal Scot

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Ger. Offen., 18 pp.

SOURCE:

CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT: 1

PAT	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE	19534744	A1	19960321	DE 1995-19534744	19950919
US	5629425	Α	19970513	US 1994-308325	19940919
IN	1995CA00614	Α	20050304	IN 1995-CA614	19950530
IN	1995CA00615	Α .	20050304	IN 1995-CA615	19950530
TW	389760	В	20000511	TW 1995-84105614	19950605
TW	412534	В	20001121	TW 1995-84105613	19950605
US	5731327	Α	19980324	US 1995-467485	19950606
EG	21479	Α	20011128	EG 1995-455	19950606
US	6399778	B1	20020604	US 1995-469093	19950606

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•	•		•			
	US 6472531	B1	20021029	US 1995-469961	19950606	
	ES 2109882	A1	19980116	ES 1995-1774	19950913	
	ES 2109882	B1	19980816			
	ES 2129293	A1	19990601	ES 1995-1775	19950913	
	ES 2129293	B1	20000116			
	NL 1001194	A1	19960319	NL 1995-1001194	19950914	
	NL 1001194	C2	19970404			
	NL 1001196	A1	19960319	NL 1995-1001196	19950914	
	NL 1001196	C2	19970404			
	ZA 9507752	A	19970314	ZA 1995-7752	19950914	
	ZA 9507753	A	19970314	ZA 1995-7753	19950914	•
	IL 115315	A	19990922	IL 1995-115315	19950914	
	IL 115314	A	20000229	IL 1995-115314	19950914	
	IL 125283 .	A	20010614	IL 1995-125283	19950914	
	IN 1995CA01111	· A	20051021	IN 1995-CA1111 CA 1995-2158399	19950914 19950915	
	CA 2158399	A1 C	19960320	CA 1995-2158399	19950915	
	CA 2158399		20010320	CA 1995-2158400	10050015	
	CA 2158400	A1 C	19960320 20061024	CM 1990-2108400	19950915	
	CA 2158400 DK 9501027	A	19960320	DK 1995-1027	19950915	
	DK 9501027 DK 175903	B1	20050606	DR 1995-1027	19950915	
	DK 175903 DK 9501028	A	19960320	DK 1995-1028	19950915	
	DK 175897	B1	20050530	DR 1993-1020	10000010	
	NO 9503657	A	19960320	NO 1995-3657	19950915	
	NO 308107	B1	20000724	NO 1993 3037	13330313	
	NO 9503658	A	19960320	NO 1995-3658	19950915	
	NO 313996	B1	20030113	2555 5655		
	SE 9503213	A	19960320	SE 1995-3213	19950915	
	SE 520721	C2	20030812			
•	SE 9503214	A	19960320	SE 1995-3214	19950915	
	SE 509265	C2	19981221	•	·	
•	RO 115259	B1	19991230	RO 1995-1619	19950915	
	RO 115260	B1	19991230	RO 1995-1620	19950915	
	CZ 290343	В6	20020717	CZ 1995-2403	19950915	
	CZ 292007	В6	20030716	CZ 1995-2402	19950915	
	FI 9504402	Α	19960320	FI 1995-4402	19950918	
	FI 112226	B1	20031114			
	FI 9504403	A	19960320	FI 1995-4403	19950918	
	FR 2724655	A1	19960322	FR 1995-10921	19950918	
	FR 2724655	B1	19971114			
	GB 2293382	A	19960327	GB 1995-19028	19950918	
	GB 2293382	В	19980819	CD 1007 1007	10050010	
	GB 2293602	A	19960403	GB 1995-19032	19950918	
	GB 2293602	В	19980506	NII 1005 21522	10050010	
•	AU 9531730	A	19960404	AU 1995-31730	19950918	
	AU 691955	B2	19980528	NII 1005 23523	10050010	
	AU 9531731	A	19960404	AU 1995-31731	19950918	
•	AU 692907	B2 `	19980618	TD 1005-229211	10050010	
	JP 08176147	A B2	19960709	JP 1995-238211	19950918	
	JP 2860071 CN 1127253	B2 A	19990224 19960724	CN 1995-118629	19950918	
	CN 1127253 CN 1075069	В	20011121	CM 1990-110023	19930910	
	JP 08193081	A	19960730	JP 1995-238209	19950918	
	LV 11177	B	19960820	LV 1995-284	19950918	
•	LV 11177 LV 11178	В	19960820	LV 1995-285	19950918	
	BR 9504059	A	19960924	BR 1995-4059	19950918	
	BR 9504060	A	19960924	BR 1995-4060	19950918	
	FR 2732020	A1 ·		FR 1995-10922	19950918	
	FR 2732020	B1	19971114			
	CN 1132205	A	19961002	CN 1995-118449	19950918	

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CN 1068324
                          R
                                20010711
     HU 74178
                          A2
                                19961128
                                            HU 1995-2723
                                                                   19950918
     HU 75033
                          A2
                                19970328
                                            HU 1995-2721
                                                                    19950918
     HU 225417
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                                20061128
     BE 1009625
                                19970603
                                            BE 1995-760
                                                                    19950918
                          Α3
                          Α3
                                19970603
                                            BE - 1995 - 761
                                                                    19950918
     BE 1009626
     RU 2104278
                          C1
                                19980210
                                            RU 1995-116242
                                                                    19950918
                          C1
                                19980410
                                            RU 1995-116238
                                                                    19950918
     RU 2108331
                                20001215
                                            AT 1995-1542
     AT 9501542
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                                                                    19950918
                                            CH 1995-2629
     CH 691125
                          A5
                                20010430
                                                                    19950918
                                20010731
                                            CH 2000-2062
     CH 691431
                          Α5
                                                                    19950918
                          Α5
                                20010731
                                            CH 1995-2628
     CH 691478
                                                                    19950918
     CH 691594
                          A5
                                20010831
                                            CH 1995-1780
                                                                    19950918
                          B1
                                20020131 PL 1995-310518
     PL 182450
                                                                    19950918
                          B1
                                            HR 1995-483
     HR 950483
                                20030228
                                                                    19950918
     PL 187686
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                                20040930
                                            PL 1995-310517
                                                                    19950918
                                            HR 1995-482
     HR 950482
                          В1
                                20070430
                                                                    19950918
     AT 502957
                          A1
                                20070615
                                            AT 1995-1543
                                                                    19950918
     WO 9609045
                          A1
                                19960328
                                            WO 1995-US11872
                                                                   19950919
         W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI,
             GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD,
             MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             TJ, TM
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
     DE 19534745
                          Α1
                                19960404
                                            DE 1995-19534745
                                                                    19950919
     DE 19534745
                          B4
                                20040609
     AU 9537186
                          Α
                                19960409
                                            AU 1995-37186
                                                                    19950919
                                            EE 1997-55
     EE 3386
                          B1
                                20010416
                                                                    19950919
     SK 283502
                          В6
                                20030805
                                            SK 1997-233
                                                                    19950919
                                            DE 1995-19549755
    DE 19549755
                         B4
                                20050504
                                                                    19950919
    DK 9700027
                         Α
                                19970109
                                            DK 1997-27
                                                                    19970109
    DK 175887.
                         B1
                                20050523
    DK 9700028
                                            DK 1997-28
                                19970109
                         Α
                                                                    19970109
     DK 175886
                          В1
                                20050523
                                20020717
     CZ 290344
                          В6
                                            CZ 2001-3548 .
                                                                   20011002
     US 2002173645
                          A1
                                20021121
                                            US 2002-83179
                                                                   20020226
PRIORITY APPLN. INFO.:
                                            US 1994-308325
                                                                A 19940919
                                            US 1995-427914
                                                                A 19950426
                                            US 1995-469093
                                                                A1 19950606
                                            IL 1995-115315
                                                                A3 19950914
                                            CZ 1995-2402
                                                                A3 19950915
                                            DE 1995-19534744
                                                                A1 19950919
                                            WO 1995-US11872
                                                                W 19950919
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AB Title compd. (I) (raloxifene hydrochloride) having a specified X-ray diffraction pattern, was prepared Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (preparation given) and 4-(2-piperidinoethoxy)benzoyl chloride hydrochloride (preparation given) in CH2Cl2 was treated with BCl3 at 0 for 8 h and at 35° for 16 h to give I.1,2-dichloroethane of 86.8% purity. The latter in MeOH was treated with NaOH and activated C followed by filtration, treatment with HCl, and crystallization to give 99.1% pure I.

L6 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1996:256453 CAPLUS Full-text

DOCUMENT NUMBER: 124:289251

TITLE: Process for preparing benzoic acid derivative intermediates and benzothiophene pharmaceutical agents

INVENTOR(S):

Kjell, Douglas Patton; Perry, Fred Mason

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 699672	A1 1996	0306 EP 1995-306050	19950830
EP 699672	B1 1998	0422	
R: AT, BE, CH,	DE, DK, ES,	FR, GB, GR, IE, IT, LI, LU,	NL, PT, SE
US 5631369	A 1997	0520 US 1994-298636	19940831
IL 128881	A 2000	1206 IL 1995-128881	19950828
CA 2157236	A1 1996	0301 CA 1995-2157236	19950830
FI 9504067	A 1996	0301 FI 1995-4067	19950830
HU 73141	A2 1996	0628 HU 1995-2537	19950830
HU 222121	B1 2003	0428	
BR 9503846	A 1996	0917 BR 1995-3846	19950830
AT 165355	T 1998	0515 AT 1995-306050	19950830
ES 2114721	T3 1998	0601 ES 1995-306050	19950830
TW 427975	B 2001	0401 TW 1995-84109069	19950830
JP 08119964	A 1996	0514 JP 1995-223183	19950831
US 5750688	A 1998	0512 US 1996-629862	19960409
PRIORITY APPLN. INFO.:		US 1994-298636	19940831
		IL 1995-115092	A3 19950828

OTHER SOURCE(S):

MARPAT 124:289251

GI

The present invention provides a novel process for prepg. novel compds. of formula HO2C(p-C6H4)O(CH2)nNR1R2 [R1, R2 = C1-C4 alkyl, combine to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compds. of formula RO2C(p-C6H4)OH [R = C1-C6 alkyl], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product of step (a) with an aqueous acid; and (c) cleaving the ester of the reaction product from step (b) to form an acid. The present invention further provides a novel process for preparing compds. of Formula I [R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidino, methylpyrrolidino, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-

hexamethyleneimino; R3, R4 = H, hydroxy protecting group; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compound of formula RO2C(p-C6H4)OH [R = C1-C6 alky], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product from step (a) with an aqueous acid; (c) cleaving the ester of the reaction product from step (b) to form an acid; (d) reacting the extracted product from step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing R3 and R4 hydroxy protecting groups of the reaction product from step (d); and (f) optionally forming a salt of the reaction from either steps (d) or step (e).

L6 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:150242 CAPLUS Full-text

DOCUMENT NUMBER:

124:202950

TITLE:

Preparation of benzothiophene glucopyranosides as

antihyperlipidemics.

INVENTOR (S):

Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom,

ADDITION NO

DATE

Terry Donald; Lugar, Charles Willis Iii; Staten,

Gilbert Stanley

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 20 pp. CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

VIND

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

DAMENIO MA

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 683170	A1	19951122	EP 1995-303265	19950516
	B1			19990310
	•		GB, GR, IE, IT, LI, LU,	אוו מיים אוו
US 5567820	л, ов, ок А	., ES, FR, 19961022		
US 6723739	B1	20040420		
CA 2149501	A1	19951121		
ZA 9503975	A			19950516
AT 184880	T			19950516
	Т3	19991201		19950516
AU 9520121	A	19951130	AU 1995-20121	19950517
AU 683734	B2	19971120		
JP 07316180	Α	19951205	JP 1995-118338	19950517
FI 9502420	Α	19951121	FI 1995-2420	19950518
NO 9501954	Α	19951121	NO 1995-1954	19950518
NO 304686	. B1	19990201		
CN 1116626	Α	19960214	CN 1995-106322	19950518
CN 1039013	В	19980708		
BR 9502079	Α	19960305	BR 1995-2079	19950518
HU 73788	A2	19960930	HU 1995-1466	19950518
HU 219335	В	20010328		
IL 113780	Α	19990620	IL 1995-113780	19950518
GR 3032142	Т3	20000427	GR 1999-403228	19991215
US 2004167080	A1	20040826	US 2004-778865	20040212
PRIORITY APPLN. INFO.:			US 1994-246655	A 19940520
				A1 19950315
	•			

OTHER SOURCE(S):

CASREACT 124:202950

AB Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-O-tetraacetyl-D-glucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

L6 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:123714 CAPLUS Full-text

DOCUMENT NUMBER:

124:155994

TITLE:

Pharmaceutical compositions containing

2-phenyl-3-aryoylbenzothiophenes for for inhibiting

Ι

bone loss and lowering serum cholesterol

INVENTOR(S):

Draper, Michael W.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Can. Pat. Appl., 31 pp.

CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2141999	<b>A1</b>	19950903	CA 1995-2141999	19950207
US 5478847	Α	19951226	US 1994-205012	19940302
ZA 9500976	Α	19960807	ZA 1995-976	19950207
NZ 314699	A	20000728	NZ 1995-314699	19950207
EP 674903	A1	19951004	EP 1995-300842	19950210
R: AT, BE, CH,	DE, DK	, ES, FR, GE	B, GR, IE, IT, LI, LU,	NL, PT, SE
NO 9500774	A	19950904	NO 1995-774	19950228
RU 2100024	C1	19971227	RU 1995-102778	19950228
RU 2150275	Cl	20000610	RU 1996-119781	19950228
AU 9513551	Α	19950907	AU 1995-13551	19950301
AU 702575	B2	19990225		
JP 07267861	Α	19951017	JP 1995-41769	19950301
JP 2818384	B2	19981030		

BR 9500784	Α	19951024	BR	1995-784		19950301
CN 1119530	A	19960403		1995-100021		19950301
CN III3330	A	19900403	CIV	1993-100021		
HU 72638	A2	19960528	HU	1995-634		19950301
JP 10291932	Α	19981104	JP	1998-107550		19950301
JP 10310525	Α	19981124	JP	1998-107549		19950301
US 5610168	Α	19970311	US	1995-422289		19950414
US 5641790	Α	19970624	US	1995-422417		19950414
US 5747510	A	19980505	US	1997-788984		19970127
US 39050	E1	20060328	US	2003-375274		20030227
PRIORITY APPLN. INFO.:			. US	1994-205012	Α	19940302
		•	JP	1995-41769	A3	19950301
•	1		US	1995-422417	A1	19950414

AB A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in postmenopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

L6 ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1995:991025 CAPLUS Full-text

DOCUMENT NUMBER:

124:106673

TITLE:

Methods for lowering serum cholesterol

INVENTOR(S):

Black, Larry J.; Bryant, Henry U.; Cullinan, George

J.; Kauffman, Raymond F.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	 A	19951107	US 1993-159159	19931130
TW 383306	В	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	A	19950615	ZA 1993-9427	19931215
				19931215
SK 279271	B6	19980805	SK 1993-1421	
IL 108042	A	19980104	IL 1993-108042	19931216
CZ 283863	В6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628		
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	C	20050614		
NO 9304740	A	19940623	NO 1993-4740	19931221
AU 9352578	Α	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		
BR 9305182	Α .	19940816	BR 1993-5182	19931221
JP 06234632	A	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	Α	19941026	CN 1993-121277	19931222
CN 1043608	В	19990616		•
AT 233559	T	20030315	AT 1993-310438	19931222

ES 2193142

PRIORITY APPLN. INFO.:

Т3 20031101 ES 1993-310438 US 1992-995222

19931222 B2 19921222

OTHER SOURCE(S):

MARPAT 124:106673

GI

$$\begin{array}{c|c} & \text{CO} & \text{OCH}_2\text{CH}_2\text{(CH}_2\text{)}_n\text{R}^2 \\ \\ \text{R}^1 & \text{I} \end{array}$$

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof. The tested compds. lowered LDL without significantly affecting primary sex targets.

ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1995:934099 CAPLUS Full-text

DOCUMENT NUMBER:

123:339764

TITLE:

SOURCE:

Processes for preparing 3-(benzoyl)-2-(4-

hydroxyphenyl) benzothiophenes

INVENTOR(S):

Dodge, Jeffrey Alan; Stocksdale, Mark Gregory

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				,
EP 675121	A1	19951004	EP 1995-302076	19950328
R: AT, BE, CH,	DE, DK	, ES, FR,	GB, GR, IE, IT, LI, LV	J, NL, PT, SE
CA 2145614	A1	19951001	CA 1995-2145614	19950327
JP 07278138	A	19951024	JP 1995-73418	19950330
US 5808061	A	19980915	US 1995-503444	19950717
PRIORITY APPLN. INFO.:			US 1994-220853	A 19940331
OTHER SOURCE(S):	CASREA	CT 123:33	9764; MARPAT 123:339764	<del>1</del>
GI				

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

The title compds. [I; R1R2 = C4-6 polymethylene, CH2CH(CH3)CH2CH2, CH2C(CH3)2CH2CH2, CH2CH2OCH2CH2] [e.g., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride], useful for the treatment of osteoporosis in post-menopausal women (no data), are prepared by: (a) coupling a benzothiophene (II; X = H) with a (hydroxyethyl)amine HOCH2CH2N(R1)R2 in the presence of P(Ph3) and di-Et azodicarboxylate; or (b) reacting a benzothiophene (II; X = CH2CH2Z; Z = leaving group) with pyrrolidine, piperidine, hexamethyleneimine, methylpyrrolidine, dimethylpyrrolidine, or morpholine; (c) deprotecting the 6-and 4-position hydroxy groups of the reaction product of step (a) or step (b); and (d) optionally salifying or forming a solvate of the reaction product of step (c).

L6 ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1995:661193 CAPLUS Full-text

DOCUMENT NUMBER:

123:111843

TITLE:

2-amino-3-aroylbenzo[b]thiophenes and methods for

preparing and using same to produce 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-aminoethoxy)benzoyl]benzo[b]thiophene

INVENTOR(S):

Godfrey, Alexander G. Eli Lilly and Co., USA

PATENT ASSIGNEE(S): SOURCE:

U.S., 9 pp.

booken.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND DATE	APPLICATION NO.	
US 5420349	A 19950530	US 1994-258641	19940610
CA 2192096	A1 19951221	CA 1995-2192096	19950607
WO 9534536	A1 19951221	WO 1995-US7399	19950607
W: AM, AT, AU,	BB, BG, BR, BY,	CA, CH, CN, CZ, DE, DK	E, EE, ES, FI,
GB, GE, HU,	IS, JP, KE, KG,	KP, KR, KZ, LK, LR, LT	, LU, LV, MD,
MG, MN, MW,	MX, NO, NZ, PL,	PT, RO, RU, SD, SE, SG	, SI, SK, TJ,
TM, TT			•
RW: KE, MW, SD,	SZ, UG, AT, BE,	CH, DE, DK, ES, FR, GB	, GR, IE, IT,
LU, MC, NL,	PT, SE, BF, BJ,	CF, CG, CI, CM, GA, GN	, ML, MR, NE,
SN, TD, TG			
AU 9528236 .	A 19960105	AU 1995-28236	19950607

EP 764150	A1 19970326	EP 1995-923804	1995060	7
EP 764150	B1 1999102	7	•	
R: AT, BE, CH,	DE, DK, ES, FR	GB, GR, IE, IT, LI, LU	J, MC, NL, E	PT, SE
HU 76000	A2 19970630	HU 1996-3404	1995060	7
HU 213834	B 19971028	3 .		
HU 76525	A2 19970925	HU 1996-3403	1995060	7
HU 216272	B 19990528	3		
BR 9507968	A 19971118	BR 1995-7968	1995060	7
JP 10503175	T 19980324	JP 1996-502366	1995060	7
AT 186050	T 1999111	AT 1995-923804	1995060	7
ES 2139222	T3 20000201	L . ES 1995-923804	1995060	7
HU 217822	B 20000428	HU 1998-2648	1995060	7
FI 9604854	A 19961204	FI 1996-4854	1996120	)4
GR 3032409	T3 20000533	GR 2000-400106	2000011	L9
PRIORITY APPLN. INFO.:		US 1994-258641	A 1994061	L <b>O</b>
		WO 1995-US7399	W 1995060	7
OTHER SOURCE(S):	CASREACT 123:1:	11843; MARPAT 123:111843	3	

A group of 2-amino-3-aroyl-benzo[b]thiophenes (I) are prepd. by prepg. an  $\alpha$ -AB hydroxy thioacetamide 4-ROC6H4CH(OH)C(:S)NR9R9 (II) wherein R, R8 and R9 independently represent C1-C6 alkyl; comprising: (a) reacting an alkyl imidate of the formula 4-ROC6H4CH(OH)C(:NH.protic acid)OR''' where R''' is C1-C6 alkyl, with a sulfur compound to yield a thioester of the formula 4-ROC6H4CH(OH)C(:S)OR'''; (b) reacting the thioester with a dialkylamine of the formula HNR8R9 to yield the  $\alpha$ -hydroxy thioacetamide; said steps being conducted without isolation or purification of the thioester., cyclizing II, and subsequently acylating the benzo[b]thiophene to yield the 2-amino-3-aryl derivative These compds. may be treated with suitable Ph Grignard reagents, and after deprotection, yield 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2piperidinoethoxy)benzoyl]benzo[b]thi ophene. %Thus, e.g., p-anisaldehyde was converted to p- methoxybenzaldehyde cyanohydrin (80% yield) and subsequently to the Me imidate 4-MeOC6H4CH(OH)C(:NH.HCl)OMe (85-90% yield); reaction of the latter with H2S/Me2NH afforded  $\alpha$ -(4-methoxy phenyl)- $\alpha$ -hydroxy- N,Ndimethylthioacetamide (70%) which was cyclized with methanesulfonic acid to 2-N, N-dimethylamino-6-methoxybenzo[b] thiophene (79%); acylation of the latter with 4-(2-piperidinoethoxy) benzoyl chloride hydrochloride (autocatalytic) afforded 2-N, N-dimethylamino-6-methoxy-3-[4-(2piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (I; R = Me, R3 = R4 = Me, R'' = 2-piperidinoethyl; 74%) which underwent Grignard reaction with 4methoxyphenylmagnesium bromide to afford 2-(4-methoxyphenyl)-6- methoxy-3-[4-(piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (90%); deprotection of the latter with AlCl3/propanethiol afforded 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thi ophene hydrochloride (95% yield).

ACCESSION NUMBER:

1995:362913 CAPLUS Full-text

DOCUMENT NUMBER:

122:213884

TITLE:

A chemical probe for the estrogen receptor: synthesis

of the 3H-isotopomer of raloxifene

AUTHOR (S):

Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C.

David

CORPORATE SOURCE:

Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

SOURCE:

Journal of Labelled Compounds & Radiopharmaceuticals

(1995), 36(1), 43-9

CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER: DOCUMENT TYPE: Wiley Journal

LANGUAGE:

English

Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of AB a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1987:433189 CAPLUS Full-text

DOCUMENT NUMBER:

107:33189

TITLE:

Treatment of mammary cancer

INVENTOR(S):

Black, Larry J.; Clemens, James A.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 10 pp. Cont. of U.S. Ser. No. 289,360,

abandoned. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

KIND APPLICATION NO. PATENT NO. DATE \_\_\_\_ \_\_\_\_\_ \_\_\_\_\_ US 1983-556875 US 4656187 Α 19870407 19831201 PRIORITY APPLN. INFO.: US 1981-289360 A1 19810803

A method of inhibiting the growth of estrogen-dependent mammary cancers comprises administering about 20 mg/kg/day of a 1st compound 6-hydroxy-2-(4hydroxyphenyl)-3-[4-(2-pyrrolidinoethoxy)benzoyl]benzo[b]th iophene (I) and .apprx.5 mg/kg/day of a 2nd compound tamoxifen (II). Also, a pharmaceutical combination comprises .apprx.4 parts by weight of I and .apprx.1 part by weight of II. I hydrochloride was prepared by reacting 4-(2pyrrolidinoethoxy) benzoic acid with thionyl chloride and then with 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene (prepared from 3-methoxybenzenethiol and  $\alpha$ -bromo-4-methoxyacetophenone). Oral doses of I 20 and II 5 mg/kg/day were given for 8 wks to rats with induced mammary tumors. Half of the rats receiving the combination treatment experienced a total regression of their tumors. The rest had only a very modest growth of their tumors during the treatment. A synergistic effect was shown.

ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN 1984:448784 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

101:48784

TITLE:

Antiestrogens. 2. Structure-activity studies in a series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic estrogenicity

AUTHOR(S):

Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.; Peters, Mary K.; Black, Larry J.; Thompson, Allen R.;

Falcone, Julie F.; Clemens, James A.

CORPORATE SOURCE:

Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

SOURCE:

Journal of Medicinal Chemistry (1984), 27(8), 1057-66

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE:

Journal

LANGUAGE:

English

GT

AB In an effort to prep. nonsteroidal antiestrogens demonstrating greater antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1984:156501 CAPLUS Full-text

DOCUMENT NUMBER:

100:156501

TITLE:

Antiestrogenic and antiandrogenic benzothiophenes

INVENTOR (S):

Jones, Charles D.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

Pacenc

DANTIN ACC. NOT

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US ^4418068	. <b>A</b>	19831129	US 1981-331042	19811216
ZA 8202247	Α	19831130	ZA .1982-2247	19820401
PRIORITY APPLN. INFO.:			US 1981-246335	A2 19810403
OTHER SOURCE(S):	CASREA	ACT 100:1565	501 ·	
GT				

AB Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un)substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2-piperidinoethoxy)benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03 µg estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

Ι

L6 ANSWER 32 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1983:422309 CAPLUS Full-text

DOCUMENT NUMBER:

99:22309

TITLE:

Acylated benzothiophenes

INVENTOR(S):

Peters, Mary K.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 246,333,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	<b>-</b> -			
US 4380635	A	19830419	US 1981-331046	19811216
CA 1167036	A1	19840508	CA 1982-400262	19820331
EP 62505	A1	19821013	EP 1982-301739	19820401

EP	62509	5			В1		19850	724					•		
	R:	AT,	BE,	CH,	DE,	FR,	GB,	IT,	LU,	NI	, SE				
GB	20966	808			Α		19821	1020	(	GB	1982	-9681			19820401
GB	20966	808			В		19850	612							
DD	20179	94			A5		19830	810	]	DD	1982	-23865	3		19820401
CS	22734	17			B2		19840	416	(	CS	1982	-2356			19820401
RO	84584	1			<b>A1</b>		19840	717	]	RO	1982	-10711	8		19820401
$\mathtt{PL}$	13058	34			B1		19840	831	:	$\mathtt{PL}$	1982	-23575	1		19820401
AT	14429	€			T		19850	815	i	ΑT	1982	-30173	9		19820401
DK	82019	513			Α		19821	1004	]	DK	1982	-1513			19820402
FI	8201	161			Α		19821	1004	]	FI	1982	-1161			19820402
JP	57183	1079			Α		19821	108		JP	1982	-56481			19820402
ES	51112	23			. A1		19830	216	]	ES	1982	-51112	3		19820402
HU	28746	5			A2		19831	L228	]	HU	1982	-1025			19820402
HU	19108	34			В		19870	128							
ຮັບ	11380	28			<b>A3</b>		19850	130	:	SU	1982	-34172	51		19820402
PRIORITY	Y APPI	LN. :	INFO	. :					1	US	1981	-24633	3	A2	19810403
	•								1	US	1981	-24633	5	Α	19810403
				•					1	US	1981	-33104	5	Α	19811216
									1	US	1981	-33104	5	Α	19811216
									1	ΕP	1982	-30173	9	Α	19820401

GI

The acylated benzothiophenones I (R,R1 = C1-4 alkyl, RR1 = polymethylene, AB CH2CHMeCH2CH2, CH2CH2OCH2CH2) were prepared by acylation-demethylation of benzothiophenes II. Thus, 3-MeOC6H4SN was treated with BrCH2COC6H4OMe-p followed by cyclization to give II, which was treated with AlCl3 and the acid chloride of 4-(2-piperidinoethoxy) benzoic acid to give I (NRR1 = piperidino).

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER:

1983:71918 CAPLUS Full-text

DOCUMENT NUMBER:

98:71918

TITLE:

Acylated benzothiophenes

INVENTOR(S):

Peters, Mary Kathleen; Jones, Charles David

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 29 pp. CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62505	A1	19821013	EP 1982-301739	19820401
EP 62505	B1	19850724		
R: AT, BE, CH,	DE, FR	, GB, IT,	LU, NL, SE	
US 4380635	Α	19830419	US 1981-331046	19811216
AT 14429	T	19850815	AT 1982-301739	19820401
PRIORITY APPLN. INFO.:			US 1981-246333 A	19810403
			US 1981-246335 A	19810403
		•	US 1981-331045 A	19811216
			US 1981-331046 A	19811216
			EP 1982-301739 A	19820401
OTHER SOURCE(S):	MARPAT	98:71918	•	

AB 3-[4-(2-Aminoethoxy)benzoyl]benzothiophenes I [R, R1 = C1-4 alkyl; RR1 = (CH2)4, (CH2)5, (CH2)6, CH2CHMeCH2CH2, CH2CH2OCH2CH2], useful as antiestrogens (no data), were prepared by acylating benzothiophene II. Thus, heating 3-MeOC6H4SCH2COC6H4OMe-4 with polyphosphoric acid gave II, which was acylated by 4-(Me2NCH2CH2O)C6H4CO2H.HCl and SOCl2 in PhCl-CH2Cl2 containing DMF and AlCl3 to give I (R = R1 = Me).

L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:71917 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER: 98:71917

TITLE: Benzothiophene compounds

INVENTOR(S): Jones, Charles David
PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 107 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: Énglish FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

GI

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62503	A1	19821013	EP 1982-301737	19820401
R: BE, CH, DE,	FR, GB	, IT, LU, NL	, SE	
AU 8282265	A	19821007	AU 1982-82265	19820401

•				US	1981-331045	A	19811216
PRIORITY APPLN. INFO.	:			US	1981-246335	Α	19810403
JP 57181081	1	Α	19821108	JP	1982-56479		19820402
GB 2097788	_	В	19850424		•		
GB 2097788		Α	19821110	GB	1982-9680		19820401
AU 555658		B2	19861002				

GI

AB [(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

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- NEWS 8 MAY 22 CA/CAplus enhanced with IPC reclassification in Japanese patents
- NEWS 9 JUN 27 CA/CAplus enhanced with pre-1967 CAS Registry Numbers
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- NEWS 14 JUL 02 SCISEARCH enhanced with complete author names
- NEWS 15 JUL 02 CHEMCATS accession numbers revised
- NEWS 16 JUL 02 CA/CAplus enhanced with utility model patents from China
- NEWS 17 JUL 16 Caplus enhanced with French and German abstracts
- NEWS 18 JUL 18 CA/CAplus patent coverage enhanced
- NEWS 19 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
- NEWS 20 JUL 30 USGENE now available on STN
- NEWS 21 AUG 06 CAS REGISTRY enhanced with new experimental property tags
- NEWS 22 AUG 06 BEILSTEIN updated with new compounds
- NEWS 23 AUG 06 FSTA enhanced with new thesaurus edition
- NEWS 24 AUG 13 CA/Caplus enhanced with additional kind codes for granted patents
- NEWS 25 AUG 20 CA/CAplus enhanced with CAS indexing in pre-1907 records

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                   RALOX-A/CN
E2
             1.
E3
             1 --> RALOXIFENE/CN
E4
               RALOXIFENE HYDROCHLORIDE/CN
E5
             1
                   RALOZAM/CN
E6
             3
                  RALSTONITE/CN
E7
                  RALSTONITE (ALF2 (OH))/CN
             1
E8
                  RALSTONITE (ALF2 (OH) .1/2H2O)/CN
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                 RALTAT 10/CN
E9
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                   RALTEGRAVIR POTASSIUM/CN
E10
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                   RALTITREXED/CN
E11
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                   RALUBEN/CN
E12
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=> s e3
             1 RALOXIFENE/CN
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L1
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN
     84449-90-1 REGISTRY
ED
     Entered STN: 16 Nov 1984
     Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-
     piperidinyl)ethoxy]phenyl] - (CA INDEX NAME)
OTHER NAMES:
CN
     Keoxifene
CN
     LY 139481
CN
     Raloxifene
     [2-(4-Hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-(2-(1-
CN
     piperidinyl) ethoxy) phenyl] methanone
MF
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CI
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LC
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       DRUGU, EMBASE, HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA,
       MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, RTECS*, SCISEARCH,
       SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:
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L2 1763 L1

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L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN

CC 1-0 (Pharmacology)

TI Osteoporosis treatment and limitations and perspectives

ST review bisphosphonate raloxifene parathyroid hormone fall prevention disuse syndrome

IT Bone, disease

(fracture; osteoporosis treatment and limitations and perspectives)

IT Anabolic agents

Osteoporosis

(osteoporosis treatment and limitations and perspectives)

IT Diphosphonates RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (osteoporosis treatment and limitations and perspectives) 13598-36-2D, Phosphonic acid, alkylidenebis-derivs. ITRL: BSU (Biological study, unclassified); BIOL (Biological study) (Bisphosphonate; osteoporosis treatment and limitations and perspectives) 9002-64-6, Parathyroid hormone IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (osteoporosis treatment and limitations and perspectives) 129318-43-0 IT 84449-90-1, Raloxifene RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (osteoporosis treatment and limitations and perspectives) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 CAPLUS COPYRIGHT 2007 ACS on STN 1763 ANSWERS L2 1-1 (Pharmacology) CC Validation of a novel HPLC method for the determination of Raloxifene and TI its pharmacokinetics in rat plasma ST Raloxifene detn plasma HPLC; liq chromatog Raloxifene plasma; pharmacokinetics Raloxifene plasma IT Blood plasma Pharmacokinetics (pharmacokinetics of Raloxifene in blood plasma of rats after oral dose) IT Blood analysis HPLC (validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma) **84449-90-1**, Raloxifene IT RL: ANT (Analyte); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study) (validation of novel HPLC method for determination of Raloxifene and its pharmacokinetics in rat plasma) HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1 L2 1763 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN CC 1-8 (Pharmacology) Effect of genistein and raloxifene on vascular dependent platelet ΤI aggregation genistein raloxifene antiplatelet platelet aggregation blood vessel ST IT Blood vessel Cardiovascular system, disease Platelet aggregation Platelet aggregation inhibitors (effect of genistein and raloxifene on vascular dependent platelet aggregation) IT Estrogen receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of genistein and raloxifene on vascular dependent platelet aggregation) Phytoestrogens IT RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT 9001-84-7, Phospholipase A2 10102-43-9, Nitric oxide, biological studies 35121-78-9, Prostacyclin

RL: BSU (Biological study, unclassified); BIOL (Biological study) (effect of genistein and raloxifene on vascular dependent platelet aggregation)

IT 446-72-0, Genistein 84449-90-1, Raloxifene

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of genistein and raloxifene on vascular dependent platelet aggregation)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1/prep

1763 L1

4449106 PREP/RL

L3

38 L1/PREP

(L1 (L) PREP/RL)

=> d 13 4 ibib abs

L3 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2005:1180831 CAPLUS Full-text

DOCUMENT NUMBER:

145:356564

TITLE:

The advance of synthetic studies on selective estrogen

receptor modulators

AUTHOR(S):

Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan

CORPORATE SOURCE:

Fourth Brigade of Pharmacy, Medical College of Chinese

People's Armed Police Force, Tianjin, 300162, Peop.

Rep. China

SOURCE:

Wujing Yixueyuan Xuebao (2005), 14(2), 151-156

CODEN: WYXUA9; ISSN: 1008-5041 Wujing Yixueyuan Xuebao Bianjibu

PUBLISHER:

Journal; General Review

DOCUMENT TYPE:

Chinese

LANGUAGE:

A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl)stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

=> d 13 ibib abs 1-

YOU HAVE REQUESTED DATA FROM 38 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2007:70746 CAPLUS Full-text

DOCUMENT NUMBER:

2007:70746 CAPLOS FULL

DOCUMENT NO

AUTHOR(S):

147:172240

TITLE:

Control of pharmaceuticals and animal health products

in wastewater effluents from manufacturing sites Parke, Neil J.; Good, Nanci F.; Meyerhoff, Roger D.

CORPORATE SOURCE:

Lilly Corporate Center, Eli Lilly and Co.,

Indianapolis, IN, 46285, USA

SOURCE:

WEFTEC.05, Conference Proceedings, Annual Technical Exhibition & Conference, 78th, Washington, DC, United States, Oct. 29-Nov. 2, 2005 (2005), 145-155. Water

Environment Federation: Alexandria, Va.

CODEN: 69JOAM

DOCUMENT TYPE:

Conference; (computer optical disk)

LANGUAGE: English

In many cases, the discharge of pharmaceuticals and animal health products at bulk manufacturing, fill/finish, development and research operations may not be directly regulated with numeric limitations as a part of a facility's wastewater discharge permit. The biol. activity of these discharged compds., if not properly managed, may have the potential to impact the operation of an onsite or a municipal wastewater treatment plant, aquatic species in streams, rivers, oceans, or a drinking water source. An overview of the Eli Lilly and Company environmental protection program is provided, which shows how potential releases of active ingredients from its operations are managed to protect the environment.

REFERENCE COUNT:

12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2006:1063108 CAPLUS Full-text

DOCUMENT NUMBER:

145:417029

TITLE:

Methods for generating stably linked complexes composed of homodimers, homotetramers or dimers of

dimers

INVENTOR (S):

Chien, Hsing Chang; Goldenberg, David M.; McBride,

William J.; Rossi, Edmund A.

PATENT ASSIGNEE(S):

IBC Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT	NO.			KIN	<b>D</b> :	DATE			APPL	ICAT	ION I	NO.		D	ATE	
		- <b></b> -			-									-		
WO 200	51076	17		A2		2006	1012	1	WO 2	006-1	US10	762		2	0060	324
W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
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	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	KM,	KN,	ΚP,	KR,
	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	MN,	MW,	MX,
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	SG,	SK,	SL,	SM,	SY,	TJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,
	VN,	YU,	ZA,	ZM,	ZW											
ŔW	: AT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,
	IS,	IT,	LT,	LU,	LV,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	SK,	TR,	BF,	ВJ,
	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝĖ,	SN,	TD,	TG,	BW,	GH,
	GM,	ΚE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
	KG,	KZ,	MD,	RU,	TJ,	TM	,									
US 200'	70869	42		A1	:	2007	0419	1	US 2	006-	4780	21		2	0060	529
WO 200'	70468	93		A2	:	2007	0426	1	WO 2	006-1	JS25	499		2	0060	529
WO 200' W:			AL,				0426 AZ,						BY,	_		
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. W:	AE, CN, GE, KR, MW, SC, US, AT, IS, CF, GM,	AG, CO, GH, KZ, MX, SD, UZ, BE, IT, CG,	CR, GM, LA, MZ, SE, VC, BG, LT, CI, LS,	AM, CU, HN, LC, NA, SG, VN, CH, LU, CM, MW,	AT, CZ, HR, LK, NG, SK, ZA, CY, LV, GA, MZ,	AU, DE, HU, LR, NI, SL, ZM, CZ, MC, GN,	AZ, DK, ID, LS, NO, SM, ZW DE, NL, GQ,	BA, DM, IL, LT, NZ, SY, DK, PL, GW,	BB, DZ, IN, LU, OM, TJ, EE, PT,	BG, EC, IS, LV, PG, TM, ES, RO, MR,	BR, EE, JP, LY, PH, TN,	BW, EG, KE, MA, PL, TR, FR, SI,	ES, KG, MD, PT, TT, GB, SK, TD,	BZ, FI, KM, MG, RO, TZ, GR, TR,	CA, GB, KN, MK, RS, UA, HU, BF, BW,	CH, GD, KP, MN, RU, UG,

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             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
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     WO 2007075270
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                                20070705
                                            WO 2006-US46367
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PRIORITY APPLN. INFO.:
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                                            US 2005-728292P
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                                            US 2006-864530P
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     The authors disclose dimerization and docking domain (DDD) sequences for the
AB
     generation of stably tethered structures of defined compns., which may have
     multiple functionalities and/or binding specificities. The tethered
     constructs may be virtually any mol. or structure, such as antibodies,
     antibody fraqments, antibody analogs or mimetics, aptamers, binding peptides,
     fragments of binding proteins, known ligands for proteins or other mols.,
     enzymes, detectable labels or tags, therapeutic agents, toxins,
     pharmaceuticals, cytokines, interleukins, interferons, radioisotopes,
     proteins, peptides, peptide mimetics, polynucleotides, RNAi, oligosaccharides,
     natural or synthetic polymeric substances, nanoparticles, quantum dots,
     organic or inorg. compds., etc. In one example, a fusion construct of a DDD
     sequence with an anti-CEA Fd fragment was prepared and shown to target
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A2

WO 2007047609

20070426

WO 2006-US40431

AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

20061016

L3 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:958171 CAPLUS Full-text

DOCUMENT NUMBER: 147:9760

TITLE: Synthesis of raloxifene hydrochloride

AUTHOR(S): Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong,

colorectal cancer in a xenograft model.

Ping

Shenyang Institute of Chemical Technology, Faculty of CORPORATE SOURCE:

Pharmaceutical-Engineering, Shenyang, 110142, Peop.

Rep. China

Zhongguo Xinyao Zazhi (2005), 14(7), 882-884 SOURCE:

CODEN: ZXZHA6; ISSN: 1003-3734

PUBLISHER:

Zhongquo Xinyao Zazhi Youxian Gongsi

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4-AB

hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3-

methoxybenzenethiol and 4-methoxy- $\alpha$ -bromo acetophenone via five steps, including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction

and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

ANSWER 4 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

2005:1180831 CAPLUS Full-text

DOCUMENT NUMBER:

145:356564

TITLE:

The advance of synthetic studies on selective estrogen

receptor modulators

AUTHOR (S):

Hu, Xiao; Zhu, Yujin; Yuan, Pengfei; Wu, Dan

CORPORATE SOURCE:

Fourth Brigade of Pharmacy, Medical College of Chinese

People's Armed Police Force, Tianjin, 300162, Peop.

Rep. China

SOURCE:

Wujing Yixueyuan Xuebao (2005), 14(2), 151-156

CODEN: WYXUA9; ISSN: 1008-5041

PUBLISHER:

Wujing Yixueyuan Xuebao Bianjibu

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

Chinese

A review on progress of synthesis of two series selective estrogen receptor modulators (SERMs): (phenyl) stilbenes and benzoheterocycles. A review on the synthesis of tamoxifen, droloxifene, raloxifene, toremifene, idoxifene, levormeloxifene and their derivs.

ANSWER 5 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:708484 CAPLUS Full-text

DOCUMENT NUMBER:

143:221841

TITLE:

Estrogen receptor ligands. Dihydrobenzoxathiin SERAMs

with an optimized antagonist side chain

AUTHOR (S):

Blizzard, Timothy A.; DiNinno, Frank; Chen, Helen Y.; Kim, Seongkon; Wu, Jane Y.; Chan, Wanda; Birzin, Elizabeth T.; Yang, Yi Tien; Pai, Lee-Yuh; Hayes, Edward C.; DaSilva, Carolyn A.; Rohrer, Susan P.;

Schaeffer, James M.; Hammond, Milton L.

CORPORATE SOURCE:

Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE:

Bioorganic & Medicinal Chemistry Letters (2005),

15(17), 3912-3916

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER:

Elsevier B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 143:221841

An optimized side chain for dihydrobenzoxathiin SERAMs was discovered and attached to four dihydrobenzoxathiin platforms. The novel SERAMs show

exceptional estrogen antagonist activity in uterine tissue and an MCF-7 breast cancer cell assay.

REFERENCE COUNT:

2.7

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

2005:451379 CAPLUS Full-text

DOCUMENT NUMBER:

142:487547

TITLE:

Antiresorptive mutual salt of raloxifene and

bisphosphonic acid

INVENTOR (S):

Ha, Tae Hee; Kim, Won Jeoung; Yun, Sangmin; Kim, Cheol Kyung; Kim, Han Kyong; Suh, Kwee-Hyun; Lee, Gwan Sun

ADDITION NO

חאתב

Hanmi Pharm. Co., Ltd., S. Korea

PATENT ASSIGNEE(S): SOURCE:

PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PA'	TENT :	NO.			KINI		DATE			APPL.					D	ATE	
WO	2005	0472	82				 2005	 0526		•					2	0041	115
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		LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	NO,
		NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,
		TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VC,	VN,	ΥU,	ZA,	ZM,	ZW	
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
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KR	2005	0468	83		Α		2005	0519	]	KR 20	003-1	8049	4		2	0031	114
EP	1689	744			A1	. :	2006	0816	]	EP 2	004-	8000	95		2	0041	115
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	ĻÏ,	LU,	ΝL,	SE,	MC,	PT,
		ΙE,	SI,	FI,	RO,	CY,	TR,	BG,	CZ,	EE,	HU,	PL,	SK,	IS			
US	2007	0828	71		A1	•	2007	0412									
PRIORIT	Y APP	LN.	INFO	. :					1	KR 20	003-1	3049	4	7	A .2	0031	114
									1	WO 20	004-1	KR29!	54	7	v 2	0041	115

MARPAT 142:487547 OTHER SOURCE(S):

The mutual salt of raloxifene and bisphosphonic acid exhibits unexpectedly synergistic effects of two components to enhance bone mineral d. (BMD), control blood-calcium d., and lower the serum cholesterol level. For example, 3.2 g of alendronic acid was mixed with 5.0 g of raloxifene in 75 mL of ethanol/75 mL of water to obtain 6.5 g of raloxifene alendronate pentahydrate. A soft or hard capsule was prepared containing raloxifene alendronate pentahydrate 30 mg, lactose 215 mg, magnesium stearate 2 mg, and colloidal silica 3 mg. When given to female rats, the mutual salt of raloxifene and alendronic acid markedly enhanced BMD, bone stiffness, trabecular volume and bone volume, and also effectively controlled the blood cholesterol and calcium level through the synergic effects of its two components, as compared with the individual raloxifene hydrochloride or alendronate.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 7 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:617920 CAPLUS Full-text

4

DOCUMENT NUMBER:

142:463529

TITLE: AUTHOR(S):

Synthesis of raloxifene hydrochloride Gong, Ping; Zhao, Yanfang; Wang, Dun

CORPORATE SOURCE:

School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop.

Rep. China

SOURCE:

Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113

CODEN: SYDXFF; ISSN: 1006-2858

PUBLISHER:

Shenyang Yaoke Daxue Xuebao Bianjibu

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

OTHER SOURCE(S):

CASREACT 142:463529

AB Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-hydroxyphenyl)benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3, saponification with 5M NaOH solution in methanol, and saltification with HCl.

The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR,

ANSWER 8 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

13C NMR.

2004:292022 CAPLUS Full-text

DOCUMENT NUMBER:

140:309411

TITLE:

L3

Pharmaceutical compositions comprising raloxifene acid

addition salts and/or solvates

INVENTOR(S):

Karup, Gunnar Leo; Pedersen, Soren Bols

PATENT ASSIGNEE(S):

A/S Gea Farmaceutisk Fabrik, Den.

SOURCE:

PCT Int. Appl., 64 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PAT	PATENT NO. KIND DATE				APPLICATION NO.						DATE						
									WO 2003-DK645						20030930		
MO.	2004	0290	46		А3		2004	1014									
•	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
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		GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KZ,	LC,	LK,
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		OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	TJ,	TM,
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							IE,										
							CM,										
CA	2499	•	•	•		•	2004		-		-	•			-	-	
AU	2003	26694	40		A1		2004	0419		AU 2	003-	2669	40		20	00309	930
	2003						2007							•			
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PRIORITY					- <del></del>								-			00209	
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OTHER SOURCE(S): MARPAT 140:309411

Raloxifene acid addn. salts or solvates thereof, having improved dissoln. properties in media comprising hydrochloric acid are described, compared with similar prepns. based on raloxifene or raloxifene-hydrochloride. disclosed acid addition salts or solvates thereof show an improved bioavailability in media comprising hydrochloric acid, such as the gastric The acid addition salts or solvates thereof are addition salts or solvates of raloxifene and a pharmaceutically acceptable acid selected among succinic acid, lactic acid, malonic acid or sulfuric acid. Further, crystalline forms of the raloxifene salts and solvates thereof are disclosed. The raloxifene acid addition salts and/or solvates thereof are useful for the preparation of pharmaceutical composition for oral administration capable of fast and reliable release of the active ingredients in the stomach of the patient, in particular for the treatment of cancer or osteoporosis, or for inhibiting cartilage degradation A new method for preparation of raloxifene lactate is also disclosed. Thus, raloxifene malonate was prepared by the reaction of raloxifene-HCl with malonic acid in propanol-water solution The product was characterized by IR spectra and x-ray diffraction.

L3 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:269853 CAPLUS Full-text

DOCUMENT NUMBER:

140:309370

TITLE:

Amino acid and peptide carriers for oral delivery of

active agent

INVENTOR(S):

Piccariello, Thomas; Kirk, Randal J.; Olon, Lawrence

Р.

PATENT ASSIGNEE(S):

New River Pharmaceuticals Inc., USA

SOURCE:

U.S. Pat. Appl. Publ., 176 pp., Cont.-in-part of U.S.

Pat. Appl. 2002 128,177.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 2

PATENT NO.	KIND DATE	APPLICATION NO.	DATE		
US 2004063628	A1 20040401	US 2002-156527	20020529		
US 7060708	B2 20060613				
WO 2000052078 .	A1 20000908	WO 2000-US5693	20000306		
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US 2002099013	A1 20020725	US 2001-933708	20010822		
US 2002128177	A1 20020912	US 2001-986426	20011108		
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The present invention relates to oral delivery systems of active agent, and more specifically to compns. that comprise amino acids, as single amino acids or peptides, covalently attached to active agents and methods for oral administration of conjugated active agent compns. For example, a polyserine-furosemide conjugate was prepared and its in vivo performance was examined Compared to parent furosemide, the conjugate showed a sustained drug release. The 9 h serum level of the polyserine-furosemide conjugate was 95.5% of its 3 h level, whereas the 9 h serum level of the parent drug was only 59.8% of its 3 h level.

L3 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2003:726588 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER:

139:345292

TITLE:

Nitrosation, nitration, and autoxidation of the selective estrogen receptor modulator raloxifene by

nitric oxide, peroxynitrite, and reactive

nitrogen/oxygen species

AUTHOR (S):

Toader, Violeta; Xu, Xudong; Nicolescu, Adrian; Yu,

CORPORATE SOURCE:

Linning; Bolton, Judy L.; Thatcher, Gregory R. J. Department of Medicinal Chemistry and Pharmacognosy,

College of Pharmacy, University of Illinois at

Chicago, Chicago, IL, 60612-7231, USA

SOURCE:

Chemical Research in Toxicology (2003), 16(10),

1264-1276

CODEN: CRTOEC; ISSN: 0893-228X

PUBLISHER:

American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

The regulation of estrogenic and antiestrogenic effects by selective estrogen AB receptor modulators (SERMs) provides the basis for use in long-term therapy in cancer chemoprevention and postmenopausal osteoporosis. However, the evidence for carcinogenic properties within this class requires study of potential pathways of toxicity. There is strong evidence for the elevation of cellular levels of NO in tissue treated with SERMs, including the benzothiophene derivative, raloxifene, in part via up-regulation of nitric oxide synthases. Therefore, the reactions of  $17\beta$ -estradiol (E2), raloxifene, and an isomer with NO, peroxynitrite, and reactive nitrogen/oxygen species (RNOS) generated from NO2-/H2O2 systems were examined Peroxynitrite from bolus injection or slow release from higher concns. of 3-morpholinosydnonimine (SIN-1) reacted with the benzothiophenes and E2 to give aromatic ring nitration, whereas peroxynitrite, produced from the slow decomposition of lower concns. of SIN-1, was relatively unreactive toward E2 and yielded oxidation and nitrosation products with raloxifene and its isomer. The oxidation and nitrosation products formed were characterized as a dimer and quinone oxime derivative Interestingly, the reaction of the benzothiophenes with NO in aerobic solution efficiently generated the same oxidation products. Stable quinone oximes are not unprecedented but have not been previously reported as products of RNOSmediated metabolism The reaction of glutathione (GSH) with the quinone oxime gave both GSH adducts from Michael addition and reduction to the corresponding o-aminophenol. The ready autoxidn. of raloxifene, observed in the presence of NO, is the first such observation on the reactivity of SERMs and is potentially a general phenomenon of significance to SERM chemical toxicol.

REFERENCE COUNT: 89 THERE ARE 89 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2003:491620 CAPLUS Full-text

DOCUMENT NUMBER: 139:179942

TITLE: Synthesis of Constrained Raloxifene Analogues by

Complementary Use of Friedel-Crafts and Directed

Remote Metalation Reactions

AUTHOR(S): Kalinin, Alexey V.; Reed, Mark A.; Norman, Bryan H.;

Snieckus, Victor

CORPORATE SOURCE: Department of Chemistry, Queen's University, Kingston,

ON, K7L 3N6, Can.

SOURCE: Journal of Organic Chemistry (2003), 68(15), 5992-5999

CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

OTHER SOURCE(S): CASREACT 139:179942

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New constrained heterocyclic analogs of Raloxifene, I [R1 = 2-(1-piperidinyl)ethoxy, R2 = H; R1 = H, R2 = 2-(1-piperidinyl)ethoxy] and II, were prepared by complementary Directed remote Metalation (DreM)/Friedel-Crafts cyclization approaches. Utilization of a benzylidene-thiolactone rearrangement was successfully implemented to construct benzothiophenes III (R3 = Me2CH, R4 = MeO; R3 = Me, PhCH2, R4 = Et2N) in good yields. Selective deprotection of III (R3 = Me2CH, R4 = MeO; R3 = PhCH2, R4 = Et2N) induced by complexation was followed by trifluoromethylsulfonylation and Suzuki-Miyaura

<sup>\*</sup> STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

cross coupling with 3-[2-(1-piperidinyl)ethoxylphenyl dioxaborolane to give the corresponding 2,4-diaryl-substituted benzothiophenes with methoxycarbonyl or diethylcarbamoyl group in the 3 position. Treatment of the latter with BCl3 or with excess LDA induced an intramol. para or ortho cyclization and concomitant double deprotection to furnish I. Similar sequence starting from III (R3 = Me, R4 = Et2N) afforded the constrained analog II.

REFERENCE COUNT:

THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

30

ACCESSION NUMBER:

2002:408662 CAPLUS Full-text

DOCUMENT NUMBER:

136:401637

TITLE:

Preparation of 3-arylbenzothiophenes by

cyclodehydration of phenylthioacetophenones using

activated clay or zeolite catalysts.

INVENTOR (S):

Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE:

PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

· PA	TENT :	NO.			KIN	D .	DATE		(2	APPL	ICAT	ION	NO.		D.	ATE	
 WO	2002	0422			7.7	-	2002		1		001-1	1042	040		-	0011	111
										WU Z	001-	0342	<b>340</b>		2	0011	T T 4
WO	2002	0422	89		<b>A3</b>		2002	0906						•			
WO	2002	0422	89		A8		2004	0212									
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
	•	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PH,	PL,
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,
		US,	UZ,	VN,	YU,	ZA,	ZW										
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	AM,	ΑZ,	BY,	KG,
		KZ,	MD,	RU,	TJ,	TM,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,
		ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,
		GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG								
AU	2002	0304	09		A5		2002	0603	7	AU 2	002-	3040	9		2	0011	114
US	2004	1327	75		A1		2004	0708	1	US 2	003-4	4155	59		2	0030	922
us	6921	827			B2		2005	0726									
PRIORIT	Y APP	LN.	INFO	. :					1	US 2	000-	2532	12P		P 2	0001	127
									1	WO 2	001-1	JS42	940	• •	W 2	0011	114
OTHER S	OURCE	(S):			CASI	REAC	T 13	5:40	1637	; MA	RPAT	136	:401	637			

II

Title compds. (I, R1, R2 = H, protecting group) were prepd. by AB cyclodehydration of phenylthioacetophenones (II; variables as above) in the presence of acid activated clays or acid activated zeolites and in the presence of solvents. Thus, PhMe,  $\alpha$ -(3-methoxyphenylthio)-4methoxyacetophenone, and "acid-activated clay" (Engelhard X-9107) were combined and refluxed 2 h using a Dean Stark trap. By HPLC the product mixture consisted of 96.7% 6-methoxy-3-(4-methoxyphenyl)benzo[b]thiophene, 1.1% 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene, 2.1% 4-methoxy-3-(4methoxyphenyl)benzo[b]thiophene, and 0.1% 4-methoxy-2-(4methoxyphenyl) benzo[b] thiophene.

L3 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2002:408636 CAPLUS Full-text

DOCUMENT NUMBER:

136:401533

TITLE:

Coupling reaction process for preparing  $\alpha$ -(3-arylthio)acetophenones from thiophenol derivs. and  $\alpha$ -(leaving group)-substituted

acetophenones

INVENTOR(S):

Luke, Wayne Douglas; Sanderson, Heidi Ann; Zheng, Hua

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE:

GI

AB

PCT Int. Appl., 17 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	CENT :	NO.			KIN	D	DATE		1	APPL	ICAT.	ION .	NO.		D	ATE		
,		2002						2002		: 1	WO 2	001-	US42	939		2	0011	114	
		-	-	-				AT,		AZ,	BA,	BB,	BG,	.BR,	BY,	BZ,	CA,	CH,	
			CN,	co,	CR,	CŪ,	CZ,	CZ,	DE,	DE,	DK,	DK,	DM,	DZ,	EC,	EE,	EE,	ES,	
			FI,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	
			KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	
	KP, KR, I MX, MZ, I					NZ,	PH,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SK,	SL,	
			TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	BY,	
			KG,	KZ,	MD,	RU													
		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪG,	ZW,	AT,	BE,	CH,	CY,	
			DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG		
	AU	2002	0285	93		A5		2002	0603		_						0011		
PRI	ORITY	APP:	LN.	INFO	. :										]				
						•									Ī	W 2	0011	114	
OTH	ER SC	URCE	(S):			CASI	REAC	T 13	<b>6:4</b> 0:	1533	; MA	RPAT	136	:401	533,				

$$R^{1}-0$$
  $S \longrightarrow 0-R^{2}$ 

 $\alpha$ -(3-Arylthio)acetophenones [I; R1, R2 = H, hydroxy-protecting group; e.g.,  $\alpha$ -(3-methoxyphenylthio)-4-methoxyacetophenone] are prepared in high yield and

selectivity by the coupling of a thiophenol derivative 3-(R10)C6H4SH (e.g., 3-methoxybenzenethiol) in an aqueous alkaline (e.g., KOH) solvent (e.g., Et acetate) with an aromatic ketone LCH2COC6H4(OR2)-4 (L = leaving group; e.g.,  $\alpha$ -chloro-4-methoxyacetophenone).

L3 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2001:283971 CAPLUS Full-text

DOCUMENT NUMBER:

134:300772 -

TITLE:

Glycosides and orthoester glycosides of raloxifene and

analogues and the use thereof

INVENTOR(S):

Holick, Michael Francis; Ramanathan, Halasya Strakan Group PLC, UK

PATENT ASSIGNEE(S):

PCT Int. Appl., 28 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:
LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT 1	NO.		•	KIN	D	DATE			APPL	ICAT	ION I	NO.		D	ATE	
						-									-		
	WO 2001	0271	29		A1		2001	0419	1	WO 2	000-	GB38	64		2	0001	006
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG;	BR,	BY,	BZ,	CA,	CH,	CN,
		CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,
		HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,
	LU, LV, M				MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,
	SD, SE, S				SI,	SK,	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UZ,	VN,
		YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM				
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZW,	AT,	BE,	CH,	CY,
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,
	DE, DK, ES CF, CG, C				CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
	GB 2355007				Α		2001	0411	(	GB 1	999-	2810	0		1	9991	126
PRIOR	ITY APP	LN.	INFO	. :					1	US 1	999-	1581	41P	:	P 19	9991	800
				•					1	US 2	000-	2315	73P		P 20	0000	911

OTHER SOURCE(S): MARPAT 134:300772

Raloxifene and raloxifene analog glycosides and orthoester glycosides afford greater serum bioavailability of the hydroxylated parent compound, and are useful for treating or preventing a number of conditions that may be treated with an anti-estrogenic or an anti-androgenic compound. To a mixture of 0.5 g raloxifene and 1.6 g silver silicate in dry acetonitrile was added 3 g mol. sieves and stirred for 20 min. To the above suspension was added 1.0 g acetobromo- $\alpha$ -D-glucose and heated for 2 h at 60°, then filtered through a bed of silica gel and eluted with dichloromethane and methanol. The yellow eluent was concentrated under vacuum to obtain yellowish crystals. Proton NMR spectrum showed the crystals were consisted of 2 possible monoglucosides and a doubly glycosylated product.

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1999:440767 CAPLUS Full-text

DOCUMENT NUMBER: 131:228604

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TITLE: Synergistic methodologies for the synthesis of 3-aroyl-2-arylbenzo[b]thiophene-based selective

estrogen receptor modulators. Two concise syntheses of

raloxifene

AUTHOR(S): Bradley, David A.; Godfrey, Alexander G.; Schmid,

Christopher R.

CORPORATE SOURCE: Chemical Process Research and Development, A Division

of Eli Lilly and Company, Lilly Corporate Center, Lilly Research Laboratories, Indianapolis, IN,

46285-4813, USA

SOURCE:

Tetrahedron Letters (1999), 40(28), 5155-5159

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER:

Elsevier Science Ltd.

DOCUMENT TYPE:

Journal

English

LANGUAGE: AB

Functionalized benzo[b] thiophene intermediates are prepd. which allow fully independent elaboration of the 2-aryl position or the tether position of benzo[b] thiophene-based selective estrogen receptor modulators (SERMs). Two

concise syntheses of the SERM raloxifene (Evista) are presented.

REFERENCE COUNT:

32

THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER:

ANSWER 16 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN 1999:188589 CAPLUS Full-text

DOCUMENT NUMBER:

130:311683

TITLE:

Novel nonsteroidal selective estrogen receptor

modulators. Carbon and heteroatom replacement of oxygen in the ethoxypiperidine region of raloxifene

AUTHOR (S):

Schmid, Christopher R.; Sluka, James P.; Duke, Kristen

M.; Glasebrook, Andrew W.

CORPORATE SOURCE:

Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN,

46285, USA

SOURCE:

Bioorganic & Medicinal Chemistry Letters (1999), 9(4),

523-528

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER:

Elsevier Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Compds. were synthesized where oxygen in the ethoxypiperidine region of raloxifene is replaced with carbon, sulfur, or nitrogen linkages. Thia- and aza-substituted compds. were prepared by novel methodol. The compds. were evaluated in vitro as selective estrogen receptor modulators (SERMs). Calcns. suggested the compds. exhibit an ER- $\alpha$  binding affinity/conformational energy relationship.

REFERENCE COUNT:

THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS 31 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3ACCESSION NUMBER:

ANSWER 17 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN 1999:71534 CAPLUS Full-text

DOCUMENT NUMBER:

130:196550

TITLE:

Nucleophilic aromatic substitution on

3-aroyl-2-arylbenzothiophenes. Rapid access to raloxifene and other selective estrogen receptor

modulators

AUTHOR (S):

Schmid, Christopher R.; Sluka, James P.; Duke, Kristin

CORPORATE SOURCE:

Lilly Research Laboratories, A Division of Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN,

46285-4813, USA

SOURCE:

Tetrahedron Letters (1999), 40(4), 675-678

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER:

Elsevier Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 130:196550

AB Versatile, mild and high yielding methods for nucleophilic arom. substitution of 2-dialkylamino-1-ethoxides and related nucleophiles on 3-aroyl-2-arylbenzothiophene nuclei are presented. A short synthesis of raloxifene is detailed.

REFERENCE COUNT:

28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1998:721690 CAPLUS Full-text

DOCUMENT NUMBER:

130:3769

TITLE:

Processes for preparing benzothiophenes

INVENTOR(S):

McGill, John McNeil, III; Misner, Jerry Wayne; Zhang,

Tony Yantao

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

SOURCE:

r. 1

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	TENT									APP:	LICAT	ION	NO.		D	ATE	
						-									-		
WC	9849	156			A1		1998	1105		WO :	1998-	US85	09		1	9980	428
	W:	AL,	AM,	AU,	AZ,	BA,	BB,	BG,	BR,	BY	, CA,	CN,	CU,	CZ,	EE,	GE,	GH,
		GM,	GW,	HU,	ID,	IL,	IS,	ĴΡ,	ΚE,	KG	, KP,	KR,	KZ,	LC,	LK,	LR,	LS,
		LT,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO	, NZ,	PL,	RO,	RU,	SD,	SG,	SI,
		SK,	SL,	TJ,	TM,	TR,	TT,	UA,	ŪĠ,	US	, UZ,	VN,	ΥU,	ZW			
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SZ,	ŪĠ,	ZW	, BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,
		GN,	ML,	MR,	NE,	SN,	TD,	TG									
CZ	2287	943			A1		1998	1105		CA :	1998-	2287	943		1	9980	428
Α	J 9872	613			Α		1998:	1124		AU :	1998-	7261	3		1	9980	428
BI	9809	439			A		2000	0613		BR :	1998-	9439			1	9980	428
н	2000	0318	7		. A2		2001	0528		HU 2	2000-	3187			1	9980	428
JI	2001	5223	72		T		2001	1113		JP :	1998-	5472	77		1	9980	428
US	6090	949			Α		2000	0718		US :	1998-	6949	7		1	9980	429 ·
EI	8755	10			A1		1998	1104		EP :	1998-	3033	74		1	9980	430
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO										
MΣ	9909	883			Α		2000	0331		MX :	1999-	9883			1	9991	
PRIORIT	Y APP	LN.	INFO	.:		•				US :	1997-	4517	7P	•	P 1	9970	430
										WO :	1998-	US85	09	1	W 1	9980	428
OTHER S	OURCE	(S):			CASI	REAC'	T 13	0:37	69;	MARI	PAT 1	30:3	769				
GT																	

#### \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; Y = Cl, Br, I, SO2(C1-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = C1-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

4

ACCESSION NUMBER:

1998:721501 CAPLUS Full-text

DOCUMENT NUMBER:

130:3768

TITLE:

Demethylation process for preparing benzo[b]thiophenes

Hoard, David Warren; Luke, Wayne Douglas

INVENTOR(S):
PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

COUDOR

Eur. Pat. Appl., 13 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

DANGUAGE.

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FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
i				
EP 875511	A1	19981104	EP 1998-303345	19980429
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IT, LI, LU, NL,	SE, MC, PT,
IE, SI, LT,	LV, FI	, RO		`
CA 2236254	A1	19981030	CA 1998-2236254	19980427
JP 11005789	. A	19990112	JP 1998-118628	19980428
US 5994547	A	19991130	US 1998-69500	19980429
PRIORITY APPLN. INFO.:			US 1997-45156P	P 19970430
OTHER SOURCE(S):	CASREA	CT 130:3768;	MARPAT 130:3768	
GI				

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

AB The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2-methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be carried out in the same reaction vessel without isolation of the acylated, protected material.

II

REFERENCE COUNT:

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:719257 CAPLUS Full-text

10

DOCUMENT NUMBER:

130:3765

TITLE:

Intermediates and processes for preparing

benzo[b] thiophenes

INVENTOR(S):

Misner, Jerry Wayne; Schmid, Christopher Randall

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT				APPLICATIO	N NO.	DATE
WO 9848	793	A1	19981105	WO 1998-US	8510	19980428
W:	AL, AM, A	T, AU,	AZ, BA, BB,	BG, BR, BY, C	A, CH, CN,	CU, CZ, DE,
	DK, EE, E	S, FI, (	GB, GE, GH,	GM, GW, HU, I	D, IL, IS,	JP, KE, KG,
	KP, KR, H	Z, LC,	LK, LR, LS,	LT, LU, LV, M	D, MG, MK,	MN, MW, MX,
	NO, NZ, I	L, PT,	RO, RU, SD,	SE, SG, SI, S	K, SL, TJ,	TM, TR, TT,
	UA, UG, U	S, UZ,	VN, YU, ZW			
RW:	GH, GM, F	Œ, LS, I	MW, SD, SZ,	UG, ZW, AT, B	E, CH, CY,	DE, DK, ES,
	FI, FR, C	B, GR,	IE, IT, LU,	MC, NL, PT, S	E, BF, BJ,	CF, CG, CI,
	CM, GA, C	N, ML, I	MR, NE, SN,	TD, TG		
CA 2287	922	A1	19981105	CA 1998-22	87922	19980428
AU 9872	614	Α	19981124	AU 1998-72	614	19980428
EP 9790	76	A1	20000216	EP 1998-91	9936	19980428
R:	AT, BE, I	E, DK,	ES, FR, GB,	GR, IT, NL, S	E, PT, IE,	FI
JP 2001	523253	Т	20011120	JP 1998-54	7278	19980428
US 6018	056	A	20000125	US 1998-69	278	19980429
PRIORITY APP	LN. INFO.:			US 1997-45	131P	P 19970430
				WO 1998-US	8510	W 19980428
OTHER SOURCE	:(S):	CASR	EACT 130:37	55; MARPAT 130	:3765	•

### \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I-III; R = hydroxy protecting group; Y = CO2H, CO2(C1-4 alkyl), C(halo), etc.; A = OH, halo, NO2, etc.; R1 = hydroxy protecting group, H], useful intermediates in the further preparation of pharmaceutical benzo[b]thiophenes, were prepared Thus, reaction of 6-methoxythianaphthen-2one with p-anisaldehyde in the presence of piperidine in EtOH and THF afforded 45% E/Z-I [R = Me].

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 21 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

5

ACCESSION NUMBER:

1998:161136 CAPLUS Full-text

DOCUMENT NUMBER:

128:221639

TITLE:

Preparation of amorphous benzothiophenes for

pharmaceuticals

INVENTOR(S):

Cuff, George W.; Thakkar, Arvind L.

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA; Cuff, George W.; Thakkar,

Arvind L.

SOURCE:

PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

P.	ATENT	NO.			KINI	)	DATE			API	P.I	CAT	ION	NO.		Ι	ATE	
-						-							7014			-	0070	
W		8513																
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							KG,											
							NZ,					SD,	SG,	SI,	SK,	ъь,	TJ,	TM,
			•	•	•	•	UZ,		-					~~	~-	~~	~	<b>~</b> 17
	RW	: GH,						UG,	ZW,	ВЕ	• ,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,
		•	MR,													_		
	P 826						1998			EP	15	97-	3064	26		]	.9970	822
E		682.																
	R:	ΑT,						FR,	GB,	GF	₹,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		•	SI,	LT,	LV,	FI,	. RO											
		3175			A1		1998	0305		CA	19	97-	2263	175		. ]	.9970	822
		2335								ΑU	19	97-	4233	5		. 1	.9970	822
A	U 723	987			B2		2000					•						
I	N 182	940 3176			A1		1999							49			.9970	
В	R 971	3176		•	Α		2000					_	1317	-			.9970	
		4124					2000										.9970	
		00117					2001	0628		HU	20	000-	1172			1	.9970	822
H	U 200	00117 839	2		<b>A3</b>		2002	0128										
N	Z 333	839			Α		2001	0629						39			.9970	
	L 128	641			Α		2001	1031		IL	19	97-	1286	41			.9970	-
		0403			T2		2002	0121									.9970	
J	P 200	25141	74				2002	0514						44			.9970	-
	T 234				T		2003	0315						26			.9970	
E	S 219	5089			Т3		2003	1201		ES	19	97-	3064	26		1	.9970	822
Z	A 970	7617			Α		1999	0225									.9970	825
U	S 671	3494			B1		2004	0330		US	19	97-	9187	41		1	9970	825
N	0 990	0914			Α		1999	0225		ИО	19	99-	914			1	.9990	225
K	R 200	00359	41		A.		2000	0626		KR	19	999-	7016	82		1	.9990	227
PRIORI	TY AP	PLN.	INFO	.:						US	19	96-	2483	1P	•	P 1	9960	828
				•						WO	19	97-1	US14	768	1	W 1	.9970	822
OWNED	COIDO	E/e).			MADI	ידית	120.	2216	2 0									

OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1997:589698 CAPLUS Full-text

DOCUMENT NUMBER:

127:272904

TITLE:

Evaluation of piperidinoethoxy moiety as an antiestrogenic substituent in non-steroidal

anti-estrogens: fertility regulation

AUTHOR(S):

Tripathi, Sachi; Dwivedy, Indra; Dhar, J. D.; Dwivedy,

Anila; Ray, Suprabhat

CORPORATE SOURCE:

Medicinal Chemistry Division, Central Drug Research

Institute, Lucknow, 226 001, India

SOURCE:

Bioorganic & Medicinal Chemistry Letters (1997),

7(16), 2131-2136

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER:
DOCUMENT TYPE:

Elsevier Journal

English LANGUAGE:

A piperidinoethoxy substituent in non-steroidal antiestrogens has a relatively AB higher antiestrogenic effect as compared to a pyrrolidinoethoxy moiety. However, the antagonistic activity is more depended on the mol. geometry than the nature of the basic chain. No significant difference in the antifertility activity in these two sets of compds. was observed

REFERENCE COUNT:

12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 23 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1997:124440 CAPLUS Full-text

DOCUMENT NUMBER:

126:144105

TITLE:

Preparation of 3-phenylbenzo[b]thiophenes

INVENTOR (S):

Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA; Hoard, David W.; Luke, Wayne

APPLICATION NO.

DATE

SOURCE:

PCT Int. Appl., 50 pp.

DATE

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

I.A.	LDIVL					_													
WO	9640	677															19	960	504
	W:	AL,	AM,	ΑT,	AU,	AZ,	BB,	BG,	BR,	, ву	, CZ	A, C	CH,	CN,	CZ,	DE	Ξ, :	DK,	EE,
		ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	, KE	e, K	G, F	œ,	KR,	KZ,	LK	ζ,	LR,	LS,
		LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	, MX	, NO	O, N	JZ,	PL,	PT,	RC	),	RU,	SD,
		SE,	SG																
	RW:	ΚE,	LS,	MW,	SD,	SZ,	UG,	ΑT,	BE,	, CH	I, DI	E, I	ρK,	ES,	FI,	FF	١, ١	GB,	GR,
		ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	, BJ	r, CI	F, C	CG,	CI,	CM,	GΑ	7		
US	5606	075			Α		1997	0225		US	1999	5-48	310:	15		•	19	9506	507
CA	2223	709			A1		1996	1219		CA	1996	6-22	223	709			19	9606	504
AU	9661	010			Α		1996	1230		AU	1996	6-61	101	)			19	9606	504
AU	7030	17			B2		1999	0311											
EP	8303	55			A1		1998	0325		ĒΡ	1996	6-91	1832	20			19	9606	504
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	, GF	2, I	Γ, Ι	JI,	LU,	NL,	SE	Ι,	PT,	·ΙΕ,
		SI,	LT,																
CN	1192	738			Α		1998	0909		CN	1996	6-19	9610	9			19	9606	504
BR	9608	851			Α														
JP	1150	7347			T		1999	0629		JP	1996	6-50	178	37			19	9606	504
HU	9900	898			A2		1999			HU	1999	9-89	8				19	9606	504
	9900						2000												
EP	1092	714			A2		2001	0418		EP	2000	0-12	820	07			19	9606	504
· EP	1092									٠.									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	, GR	2, I	Г, І	ĿΙ,	LU,	ΝL,	SE	Ξ,	PT,	ΙE,
			LT,																
	1221																		
	9705				Α		1998	0127											
PRIORIT	Y APP	LN.	INFO	.:										15					
														20					
										WO	1996	6 - US	947	77		W	19	9606	504
OTHER SO	DURCE	(S):			MARI	PAT	126:	1,441	05										

GI

$$R^{1}$$
  $R^{2}$   $R^{2}$ 

AB Title compds. [I; R1,R2 = H, halo, (aryl)alkoxy, NH2] were pred. by cyclization of 4-R1C6H4CH:C(SR4)C6H4R2-4 [R4 = trialkylsilyloxy, (di)(alkyl)amino, alkylthio, etc.] in the presence of an acid.

L3 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:740256 CAPLUS Full-text

DOCUMENT NUMBER:

126:7985

TITLE:

Preparation of 3-[4-(2-heterocyclylethoxy)benzoyl-2-

phenylbenzothiophenes for use in alleviating the

symptoms of post-menopausal syndrome

INVENTOR (S):

Dodge, Jeffrey Alan; Jones, Charles David; Bourgeois,

Tokarz Michelle Lee

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 67 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA.	TENT :	NO.			KINI	D	DATE			APPI	ICAT	ION 1	ио.		D.	ATE	
	7387 7387						1996 1997			EP 1	.996-	3027	13		1	9960	418
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	İT,	LI,	NL,	PT,	SE
US	6608	090			B1		2003	0819	. 1	US 1	995-	4265	52		1	9950	421
CA	2215	902			A1		1996	1024		CA 1	996-	2215	902		1	9960	418
WO	9632	937			A1		1996	1024	1	WO 1	.996-1	US53	82		1	9960	418
	W:	AL,	AM,	AU,	ΑZ,	BB,	BG,	BR,	BY,	CA,	CN,	CZ,	EE,	GE,	HU,	IS,	JP,
		ΚE,	KG,	KP,	KR,	KZ,	LK,	LR,	LS,	LT,	LV,	MD,	MG,	MK,	MN,	MW.,	MX,
		NO,	NZ,	PL,	RO,	RU,	SD,	SG,	SI,	SK,	ТJ,	TM,	TR,	TT,	UA,	ŪĠ,	US,
		US,	UZ								•						
	RW:	KΕ,	LS,	MW,	SD,	SZ,	ŬĠ,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML,	MR,
	•	ΝE,	SN,	TD,													
AU	9655	549			Α		1996	1107		AU 1	.996-	5554	9		1	9960	418
JP	1150	4013			T		1999	0406	,	JP 1	996-	5319	11		1	9960	418
PRIORITY	Y APP	LN.	INFO	.:					1	US 1	.995-	4263	39	1	A 1	9950	421
									1	US 1	.995-	4265	52	2	A 1	9950	421 .
									1	WO 1	.996-1	US538	82	V	N 1	9960	418
OTHER SO	OURCE	(S):			MARI	PAT	126:	7985									

GI

$$\mathbb{R}^{1}$$
 $\mathbb{R}^{2}$ 
 $\mathbb{R}^{2}$ 
 $\mathbb{R}^{2}$ 

The title compds. [I; R1, R2 = H, OH, alkoxy, etc.; R3 = (substituted) AB pyrrolidino, piperidino, piperazino, etc.], useful in alleviating the symptoms of post-menopausal syndrome related to osteoporosis, cardiovascular disease, hyperlipidemia, estrogen-dependent cancer, and in alleviating the symptoms of uterine fibroid disease, endometriosis, aortal smooth muscle cell proliferation, and restenosis, were prepared and formulated. Thus, reaction of bromide II with 3-phenylpyrrolidine in DMF followed by demethylation with EtSH/AlCl3 in CH2Cl2 afforded I [R1, R2 = H; R3 = 3-Ph-pyrrolidin-1-yl] which reduced 63.4% serum cholesterol at 10 mg/kg.

CAPLUS COPYRIGHT 2007 ACS on STN ANSWER 25 OF 38 L3

ACCESSION NUMBER:

1996:672963 CAPLUS Full-text

DOCUMENT NUMBER:

126:7983

TITLE:

Process for the synthesis of benzo[b]thiophenes

INVENTOR(S):

Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE:

U.S., 10 pp. CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PAT	CENT 1	NO.			KIND DATE				2	APPL	ICAT	ON I	NO.		D	ATE	
						_									-		
US	5569	772			Α		1996	1029	1	JS 1	995-	4868	73		1:	9950	607
CA	2223	681			A1		1996	1219	(	CA 1	996-	2223	681		1	9960	604
WO	9640	678			A1		1996	1219	1	WO 1	996-1	US93.	57		1:	9960	604
	W:	AL,	AM,	AT,	AU,	ΑZ,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,
		ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LK,	LR,	LS,
		LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,
		SE,	SG					•									
	RW:	KE,	LS,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,
		ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA		
ΑU	9660	970			Α		1996	1230		AU 1	996-	6097	0		1:	9960	604
ΑU	6985	58			B2		1998	1029									
ΕP	8303	56			<b>A1</b>		1998	0325	]	EP 1:	996-	9182	77		1:	9960	604
EР	8303	56			B1		2001	0822			`						
1	·R:	AT.	BE.	CH,	DE.	DK.	ES.	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	PT,	IE,

SI, LT, LV,	FI	•		·		
CN 1192212	Α	19980902	CN	1996-195899		19960604
BR 9609156	Α	19990629	BR	1996-9156		19960604
JP 11507338	T	19990629	JP	1997-501694		19960604
HU 9900903	. A2	19990728	HU	1999-903		19960604
HU 9900903	<b>A</b> 3	20010129				
IL 122091	A	20010520	IL	1996-122091		19960604
AT 204575	T	20010915	AT	1996-918277		19960604
ES 2159742	T3	20011016	ES	1996-918277		19960604
PT 830356	${f T}$	20011228	PT	1996-918277		19960604
NO 9705579	Α	19971203	NO	1997-5579		19971203
PRIORITY APPLN. INFO.:			US	1995-486873	Α	19950607
			WO	1996-US9357	W	19960604

OTHER SOURCE(S):

CASREACT 126:7983; MARPAT 126:7983

GI

$$R^1$$
 $R^2$ 
 $R^2$ 

AB The title compds. I [R1, R2 = H, alkoxy, etc.] are prepd. Thus, treatment of (E)-tert-Bu 4,4'-dimethoxystilbenyl sulfoxide with p-toluenesulfonic acid in refluxing toluene gave, after workup and purifn, (E)- and (Z)-I [R1 = R2 = MeO].

L3 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:649600 CAPLUS Full-text

DOCUMENT NUMBER:

125:266032

TITLE:

Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal

syndrome-associated indications and estrogen-dependent

diseases, and pharmaceuticals containing them

INVENTOR(S):

Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey

s.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 19 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

		•		
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 729964	A1	19960904	EP 1996-300878	19960209
ED 729964	R1	20010509		

	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IE,	IT,	LI,	LU,	NL,	PT,	SE
US	6479	517			B1		2002	1112		US	1995-	3959	44		1	9950	228
ES	2158	242			Т3		2001	0901		ES	1996-	3008	78		1	9960:	209
CA	2169	414			<b>A1</b>		1996	0829		CA	1996-	2169	414		1	9960:	213
JP	0825	9560			Α		1996	1008		JΡ	1996-	2528	1		1	9960	213
US	5998	443			Α		1999	1207		US	1997-	9468	42		1	9971	800
PRIORITY	APP	LN.	INFO.	:						US	1995-	3959	44	7	A 1	9950:	228
OTHER SO	URCE	(S):			MARP	ΉT	125:	26603	32								
GI																	

Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(O-alkyl)2, OPO(O-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds. of the invention, as well as pharmaceutical compns. containing compds. of the invention.

L3 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:333087 CAPLUS Full-text

DOCUMENT NUMBER: 125:86485

TITLE: Prepn. of vinyl sulfenic acid derivatives for

benzo[b] thiophene synthesis

INVENTOR(S): Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 13 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

LANGUAGE: Englis
FAMILY ACC. NUM. COUNT: 2

PATENT NO.	KIND ·	DATE	APPLICATION NO.	DATE
US 5514826	Α	19960507	US 1995-483607	19950607
CA 2224225	A1	19961219	CA 1996-2224225	19960604
WO 9640693	A1	19961219	WO 1996-US9460	19960604

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM AU 9661003 Α 19961230 AU 1996-61003 19960604 AU 698076 B2 19981022 19980325 EP 1996-918314 19960604 EP 830362 A1 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, R: SI, LT, LV, FI CN 1996-195947 19960604 Α 19980902 CN 1192215 CN 1068883 В 20010725 BR 9608847 Α 19990608 BR 1996-8847 19960604 T 19990629 JP 1997-501774 19960604 JP 11507346 HU 9900923 A2 19990728 HU 1999-923 19960604 **A3** 20000228 HU 9900923 Α 20010520 IL 1996-122127 19960604 IL 122127 NO 9705633 Α 19980128 NO 1997-5633 19971204 20001212 20020109 CN 2000-130796 CN 1330071 Α 19950607 PRIORITY APPLN. INFO.: US 1995-482692 Α US-1995-483607 19950607 Α WO 1996-US9460 W 19960604

The present invention is directed to novel vinyl sulfenic acid derivs. I [R1, R2 = H, alkoxy, arylalkoxy, halo, amino; R4 = OSi(R3)3, NR5R6, SR8; R5and/or R6 = H, alkyl, arylalkyl, aryl, -(CH2)5-, -(CH2)4-, -(CH2)2O(CH2)2-, -(CH2)6-; R8 = alkyl, aryl, arylalkyl useful for the synthesis of benzo[b]thiophenes, in particular 2-arylbenzo[b]thiophenes. E.g., desoxyanisoin reacts with 2-methyl-2-propanethiol to give I [R1 = R2 = OMe; R4 = C(Me)3] which in turn cyclizes to 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene.

L3 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:256454 CAPLUS Full-text

DOCUMENT NUMBER:

124:289252

TITLE:

GI

Process for preparing benzoic acid derivative

intermediates and benzothiophene pharmaceutical agents

INVENTOR(S):

Kjell, Douglas Patton

Ι

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 16 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 699673	A1	19960306	EP 1995-306053	19950830

EP	6996	73			B1	1	1998	0422									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	R, IE	, IT	, LI,	LU,	NL	, PT,	SE
US	5731	436			Α	1	1998	0324	Ü	JS	1994	-298	891			19940	831
IL	1150	91			Α	2	2000	0831	I	ΓL	1995	-115	091			19950	828
IL	1265	93			Α	2	2000	0831	I	ΓL	1995	-126	593			19950	828
CA	2157	235			<b>A1</b>	1	1996	0301	C	CA	1995	-215	7235			19950	830
FI	9504	068			Α	1	1996	0301	F	T	1995	-406	8			19950	830
HU	7313	6			A2	1	1996	0628	H	ΙU	1995	-253	9			19950	830
BR	9503	847			Α	1	1996	0917	E	3R	1995	-384	7 .			19950	830
AΤ	1653	56			${f T}$	1	L998	0515	P	lΥ	1995	-306	053			19950	0830
ES	2114	722			Т3	1	L998	0601	E	ΞS	1995	-306	053			19950	830
JP	0811	9912			Α	1	1996	0514	J	JP	1995	-223	184			19950	831
US	5955	80,6			A	1	1999	0921	τ	JS	1998	-167	61			19980	130
PRIORITY	APP	LN.	INFO	. :					τ	JS	1994	-298	891		A	19940	831
									. ]	ĽL	1995	-115	091		Α3	19950	828
		\															

OTHER SOURCE(S): MARPAT 124:289252

GI

The present invention provides a novel process for prepg. a compd. of formula AB RO2C(p-C6H4)O(CH2)nNR1R2 [R = C1-C4 alkyl; R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2(p-C6H4)O(CH2)nOH [R and n are as defined above, with a leaving group donor]; and (c) reacting the product of step (b), a compound of formula RO2(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneamine]. The product of the above process also is novel and is useful for the preparation of pharmaceutically active compds. of formula I, particularly via the following novel process [R = C1-C4 alkyl; R1 and R2 each are independently C1-C4 alkyl, or combine to form piperidinyl, pyrrolidinyl, methylpyrrolidino, dimethylpyrrolidino, morpholino, dimethylamino, diethylamino, of 1-hexamethyleneimino; n = 2, 3; or a pharmaceutically acceptable salt thereof, comprising (a) condensing (C1-C4 alkyl) 4-hydroxybenzoate with ethylene carbonate or propylene carbonate in the presence of a condensation catalyst and a moderately polar, water immiscible solvent having a high b.p.; (b) reacting the product of step (a), a compound of formula RO2C(p-C6H4)O(CH2)nOH [R and n are as defined above, with the leaving group donor]; (c) reacting the product of step (b), a compound of formula RO2C(p-C6H4)O(CH2)nX [R and n are as defined above; X = leaving group

with a base selected from the group consisting of piperidine, pyrrolidine, methylpyrrolidine, dimethylpyrrolidine, morpholine, dimethylamine, diethylamine, and 1-hexamethyleneimine]; (d) reacting the product of step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing the reaction product from step (d); and (f) optionally forming a salt of the reaction product from either step (d) or step (e).

L3 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:237478 CAPLUS Full-text

DOCUMENT NUMBER:

124:289249

TITLE:

An improved process for preparing 3-(4-aminoethoxybenzoyl)benzo[b]thiophenes

INVENTOR(S):

Alt, Charles Arthur Eli Lilly and Co., USA

PATENT ASSIGNEE(S): SOURCE:

Eli Lilly and Co., USA Eur. Pat. Appl., 15 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 693488	A1 19960124	EP 1995-305085	19950720
EP 693488	B1 20010919		
R: AT, BE, CH,	DE, DK, ES, FR,	GB, GR, IE, IT, LI, LU,	NL, PT, SE
US 5523416	A 19960604	US 1995-422294	19950414
HU 71596	A2 19960129	HU 1995-2176	19950719
AU 9525068	A 19960201	AU 1995-25068	19950719
AU 684181	B2 19971204	L .	
ZA 9506031	A 19970120	ZA 1995-6031	19950719
CA 2154319	A1 19960123	CA 1995-2154319	19950720
FI 9503513	A 19960123	FI 1995-3513	19950720
NO 9502891	A 19960123	NO 1995-2891	19950720
CN 1116624	A 19960214	CN 1995-109618	19950720
JP 08053440	A 19960227	JP 1995-183923	19950720
IL 114684	A 19990620	IL 1995-114684	19950720
AT 205842	T 20011015	AT 1995-305085	19950720
ES 2160668	T3 20011116	ES 1995-305085	19950720
PT 693488	T 20020228	B . PT 1995-305085	19950720
BR 9503408	A 19960227	BR 1995-3408	19950721
US 5512684	A 19960430	US 1995-512724	19950808
PRIORITY APPLN. INFO.:		US 1994-279456	A 19940722
		US 1995-422294	A1 19950414

OTHER SOURCE(S):

CASREACT 124:289249; MARPAT 124:289249

GI

A process for prepg. 6-alkoxy-3-(4-alkoxyphenyl)benzo[b]thiophenes (I; A = H; AB R = same or different C1-6 alkyl) in good yield on a manufacturing scale without generating a thick, potentially yield-reducing, paste and thereby without mixing problems, involves intramol. cyclization of  $\alpha$ -(3alkoxyphenylthio)-4-alkoxyacetophenones (II; R = same as above). invention also provides methods for converting  $\alpha$ -(alkoxyphenylthio)-4alkoxyacetophenones I (A = H; R = same as above) into 6-hydroxy-2-(4hydroxyphenyl) -3-[4-(2- aminoethoxy) benzoyl] benzo[B] thiophenes I (A = Q, R = H; R5 = NR1R2; wherein R1, R2 = C1-4 alkyl, or R1R2 = C4-6 polymethylene or CH2CH2OCH2CH2) via acylation of a dialkoxy benzo[b]thiophene I (A = H; R = same as above) with an acylating agent R4-Q (R4 = C1, Br, an active ester, etc.; R5 = same as above) under Friedel-Crafts conditions. bromo-4-methoxyacetophenone was added portion-wise to a mixture of 100 g 4methoxybenzenethiol and 39 g KOH in 300 mL and denatured EtOH in a cooling and stirred for 10 min in the cooling bath and at ambient temperature for 3 h to give, after workup, 158 g  $\alpha$ -(3-methoxyphenylthio)-4- methoxyacetophenone. The latter compound (6.92 g) was added steadily over 1/2 h to a mixture of 41.5 g polyphosphoric acid and 13.8 g phosphoric acid and the reaction mixture was heated at 85° for 1.75 h and cooled to 50°, to give , after extraction with toluene and crystallization, the desired 6-isomer, I (A = H, R = Me) (69% yield). The latter compound (30 g) was heated with 90 g pyridine hydrochloride with stirring at 210° for 30 min to give, after workup, 25.5 g I (A = R = H), which (40 g) was acetylated by Ac2O in the presence of 4dimethylaminopyridine in pyridine to give 52.5 g I (A = H, R = Ac). This compound (20 q) was added to a solution of 4-(2-piperidinoethoxy)benzoyl chloride (prepared from 16.3 g of the benzoic acid derivative) in ClCH2CH2Cl and stirred vigorously, followed by adding 73.4 g AlCl3 over 3 min, and the resulting mixture was stirred for 1 h to give, after workup, the desired product I [A = Q (wherein R5 = piperidino), R = Ac] as an oil, which was saponified with a mixture of 275 mL MeOH and 55 mL 5 n aqueous NaOH under reflux to give 10.5 g the title compound I [A = Q, wherein R5 = piperidino, R = H].

ANSWER 30 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN 1996:150242 CAPLUS Full-text

ACCESSION NUMBER:

DOCUMENT NUMBER: 124:202950

TITLE: Preparation of benzothiophene glucopyranosides as

antihyperlipidemics.

Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom, INVENTOR(S):

Terry Donald; Lugar, Charles Willis Iii; Staten,

Gilbert Stanley

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

		DATE	APPLICATION NO.	DATE
EP 683170	A1	19951122	EP 1995-303265	19950516
EP 683170	B1	19990922		
R: AT, BE, CH,	DE, DK	ES, FR,	GB, GR, IE, IT, LI, LU,	NL, PT, SE
US 5567820			US 1995-404701	19950315
US 6723739	B1 ·	20040420	US 1995-405555	19950315
CA 2149501	A1	19951121	CA 1995-2149501	19950516
ZA 9503975	Α	19961118	ZA 1995-3975	19950516
AT 184880	T	19991015	AT 1995-303265	19950516
ES 2136799	Т3	19991201	ES 1995-303265	19950516
AU 9520121	Α	19951130	AU 1995-20121	19950517
AU 683734		19971120	•	
JP 07316180	A	19951205	JP 1995-118338	19950517
FI 9502420	Α	19951121	FI 1995-2420	19950518
	Α	19951121	NO 1995-1954	19950518
NO 304686	B1	19990201		
CN 1116626	Α	19960214	CN 1995-106322	19950518
CN 1039013	В	19980708		
BR 9502079	Α	19960305	BR 1995-2079	19950518
HU 73788	A2	19960930	HU 1995-1466	19950518
HU 219335	B	20010328		
· IL 113780		19990620	IL 1995-113780	19950518
GR 3032142	Т3	20000427	GR 1999-403228	19991215
US 2004167080	A1	20040826	US 2004-778865	20040212
PRIORITY APPLN. INFO.:	'		US 1994-246655	A 19940520
			US 1995-405555	
OBUED COUNCE/C).	CACDEA	CT 124.20	2050	

OTHER SOURCE(S):

CASREACT 124:202950

GI

AB

Raloxifene metabolites (I) and (II) and their hydrochloride salts were prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene

and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-0-tetraacetyl-Dglucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

ANSWER 31 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:123714 CAPLUS Full-text

DOCUMENT NUMBER:

124:155994 .

TITLE:

Pharmaceutical compositions containing

2-phenyl-3-aryoylbenzothiophenes for for inhibiting

APPLICATION NO.

DATE

bone loss and lowering serum cholesterol

INVENTOR(S):

Draper, Michael W.

DATE

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Can. Pat. Appl., 31 pp. CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

	CA 2141999	A1	19950903	CA 1995-2141999	19950207
		A	19951226	US 1994-205012	19940302
	ZA 9500976	A	19960807	ZA 1995-976	19950207
	NZ 314699	Α	20000728	NZ 1995-314699	19950207
	EP 674903	A1	19951004	EP 1995-300842	19950210
	R: AT, BE, C	H, DE, DK	, ES, FR,	GB, GR, IE, IT, LI, LU,	NL, PT, SE
	NO. 9500774	Α	19950904	NO 1995-774	19950228
	RU 2100024	C1	19971227	RU 1995-102778	19950228
	RU 2150275	C1	20000610	RU 1996-119781	19950228
	AU 9513551	A	19950907	AU 1995-13551	19950301
	AU 702575	B2	19990225		
`	JP 07267861	Α	19951017	JP 1995-41769	19950301
	JP 2818384	B2	19981030		
٠.	BR 9500784	A	19951024	BR 1995-784	19950301
	CN 1119530	· A	19960403	CN 1995-100021	19950301
	HU 72638	. A2	19960528	HU 1995-634	19950301
•	JP 10291932	Α	19981104	JP 1998-107550	19950301
•	JP 10310525	Α	19981124	JP 1998-107549	19950301
	US 5610168	Α	19970311	US 1995-422289	19950414
	US 5641790	A	19970624	US 1995-422417	19950414
	US 5747510	Α	19980505	US 1997-788984	19970127
,	US 39050	E1	20060328	US 2003-375274	20030227
PRIC	RITY APPLN. INFO.:			US 1994-205012	A 19940302
				JP 1995-41769	A3 19950301
		•		US 1995-422417	A1 19950414
AB	A method of inhil	oiting bor	ne loss or	resorption, or lowering	serum chole

A method of inhibiting bone loss or resorption, or lowering serum cholesterol, comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in postmenopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

ANSWER 32 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3 1995:991025 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

124:106673

Methods for lowering serum cholesterol

INVENTOR(S): Black, Larry J.; Bryant, Henry U.; Cullinan, George

J.; Kauffman, Raymond F.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

GI

English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	Α .	19951107	US 1993-159159	19931130
TW 383306	В	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	Α	19950615	ZA 1993-9427	19931215
SK 279271	В6	19980805	SK 1993-1421	19931215
IL 108042	Α	19980104	IL 1993-108042	19931216
CZ 283863	B6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628		
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	C	20050614		
NO 9304740	A	19940623	NO 1993-4740	19931221
AU 9352578	Α	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		
BR 9305182	Α	19940816	BR 1993-5182	19931221
JP 06234632	Α	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	$\mathbf{A}$	19941026	CN 1993-121277	19931222
CN 1043608	В	19990616	•	
AT 233559	T	20030315	AT 1993-310438	19931222
ES 2193142	Т3	20031101	ES 1993-310438	19931222
PRIORITY APPLN. INFO.:			US 1992-995222.	B2 19921222
OTHER SOURCE(S):	MARPAT	124:106673		

$$\begin{array}{c|c} & \text{CO} & \text{OCH}_2\text{CH}_2\text{(CH}_2\text{)}_n\text{R}^2 \\ \\ \text{R}^1 & \text{I} \end{array}$$

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof. The tested compds. lowered LDL without significantly affecting primary sex targets.

L3 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1995:362913 CAPLUS Full-text

DOCUMENT NUMBER: 122:213884

TITLE: . A chemical probe for the estrogen receptor: synthesis

of the 3H-isotopomer of raloxifene

AUTHOR(S): Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C.

David

CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals

(1995), 36(1), 43-9

CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate

was accessed by regioselective aroylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1-

piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me

ethers in the presence of the ethoxy side-chain followed by palladium

catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L3 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1994:700754 CAPLUS Full-text

DOCUMENT NUMBER: 121:300754

TITLE: [[(Alkylsulfonyl)oxy]benzo[b]thienyl]methanones and

[[(aminocarbonyl)oxy]benzo[b]thienyl]methanones

pharmaceuticals

INVENTOR(S): Black, Larry John; Bryant, Henry Uhlman; Cullinan,

George Joseph

PATENT ASSIGNEE(S): Eli Lilly and Co., USA SOURCE: Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
	617030	A1	19940928	EP 1994-301871	19940316
ΕP	617030	B1	19990526	•	•
	R: AT, BE, CH	, DE, DK	, ES, FR,	GB, GR, IE, IT, LI, LU,	NL, PT, SE
US	5482949	Α	19960109	US 1993-35121	19930319
$z_{A}$	9401786	A	19950914	ZA 1994-1786	19940314
CA	2119091	A1	19940920	CA 1994-2119091	19940315
NO	9400940	A	19940920	NO 1994-940	19940316
ΑU	9457863	A	19940922	AU 1994-57863	19940316
ΑU	670177	B2	19960704		
BR	9401183	Α.	19941101	BR 1994-1183	19940316
HU	70549	A2	19951030	HU 1994-774	19940316
ΑT	180479	· <b>T</b>	19990615	AT 1994-301871	19940316
ES	2132339	Т3	19990816	ES 1994-301871	19940316
FI	9401262	Α	19940920	FI 1994-1262	19940317
JP	06321937	Α .	19941122	JP 1994-47091	19940317

CN 1097420	Α	19950118	CN	1994-102910		19940317
US 5994371	Α	19991130	US	1995-392445		19950222
US 5599833 ·	Α	19970204	US	1996-588670		19960117
US 5605924	Α	19970225	US	1996-588663		19960117
US 5798351	Α	19980825	US	1997-958535		19971027
PRIORITY APPLN. INFO.:			US	1993-35121	Α	19930319
			US	1995-392445	A3	19950222

OTHER SOURCE(S):

MARPAT 121:300754

GI

### \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The (4-alkoxybenzoyl)benzo[b]thiophene-6-sulfonates and (4-AB alkoxybenzoyl)benzo[b]thien-6-yl carbamates I (R = OH, alkoxysulfonyl, carbamoyl; R1 = H, OH, halo, etc.; R2 = pyrrolidino, piperidino, etc.; X = bond, methine) were disclosed as agents for inhibiting the loss of bone, lowering serum cholesterol levels and therapeutically treating hormone dependent mammalian breast and uterine carcinoma. A specifically claimed example compound is [6-[(pentylsulfonyl)oxy]-2-[4-[(pentylsulfonyl)oxy]phenyl]benzo[b]thien-3-yl][4-[2-(1piperidinyl)ethoxy]phenyl]methanone (II).

L3 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:448784 CAPLUS Full-text

DOCUMENT NUMBER: 101:48784

2. Structure-activity studies in a TITLE: Antiestrogens.

series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone hydrochloride (LY 156758), a remarkably effective

estrogen antagonist with only minimal intrinsic

estrogenicity

Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.; AUTHOR(S):

Peters, Mary K.; Black, Larry J.; Thompson, Allen R.;

Falcone, Julie F.; Clemens, James A.

CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

Journal of Medicinal Chemistry (1984), 27(8), 1057-66 SOURCE:

CODEN: JMCMAR; ISSN: 0022-2623

Journal DOCUMENT TYPE:

LANGUAGE: English

GΙ

Ι

In an effort to prep. nonsteroidal antiestrogens demonstrating greater antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b] thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino) ethoxy side chain functionality elsewhere in the mol. was AlCl3/EtSH. The benzothiophene derivs. were tested for their ability to inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

ANSWER 36 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN L3

ACCESSION NUMBER:

1984:156501 CAPLUS Full-text

DOCUMENT NUMBER:

100:156501

TITLE:

Antiestrogenic and antiandrogenic benzothiophenes

INVENTOR(S):

Jones, Charles D.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	AP:	PLICATION NO.		DATE
US 4418068	. <b>A</b>	19831129	US	1981-331042		19811216
ZA 8202247	Α	19831130	ZA	1982-2247		19820401
PRIORITY APPLN. INFO.:			US	1981-246335	A2	19810403
OTHER SOURCE(S):	CASRE	ACT 100:1565	0 1 <sup>.</sup>			
GI	•					

Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es AB I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un)substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2piperidinoethoxy) benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered 0.03  $\mu g$  estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

L3 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1983:71917 CAPLUS Full-text

DOCUMENT NUMBER:

98:71917

TITLE:

Benzothiophene compounds

INVENTOR (S):

Jones, Charles David

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 107 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP	62503	A1	19821013	EP 1982-301737	19820401
	R: BE, CH, DE,	FR, GB	, IT, LU, NL	, SE	
· AU	8282265	Α	19821007	AU 1982-82265	19820401
AU	555658	B2	19861002		
GB	2097788	A	19821110	GB 1982-9680	19820401
GB	2097788	В	19850424		
JP	57181081	A	19821108	JP 1982-56479	19820402
PRIORITY	APPLN. INFO.:			US 1981-246335 A	19810403
				US 1981-331045 A	19811216

GI

[(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).

L3 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1983:71916 CAPLUS Full-text

DOCUMENT NUMBER: 98:71916

TITLE: 3-(4-Aminoethoxybenzoyl)benzo[b]thiophenes

חאייים

INVENTOR(S): Jones, Charles David; Goettel, Mary Elizabeth

PATENT ASSIGNEE(S): Eli Lilly and Co., USA SOURCE: Eur. Pat. Appl., 59 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

DATENIT NO

PAT	TENT NO.			KIND	DATE	APPLICATION NO.		DATE
	62504			A1	19821013	EP 1982-301738		19820401
EP	62504	D.F.	<b>CIT</b>	B1	19860102	THE NEW COS		
	•	BE,	CH,	•		LU, NL, SE		
	4358593			Α	19821109			19810403
IL	65378			A	19860228			19820330
CA	1167037			A1	19840508	CA 1982-400300		19820331
GB	2097392			Α	19821103	GB 1982-9679		19820401
GB	2097392			В	19850424			
DD	201793			. A5	19830810	DD 1982-238654		19820401
CS	227348			B2	19840416	CS 1982-2357		19820401
$\mathtt{PL}$	130867			B1	19840929	PL 1982-235752		19820401
AT	17243			T	19860115	AT 1982-301738		19820401
DK	8201512			A	19821004	DK 1982-1512		19820402
FI	8201160			A	19821004	FI 1982-1160		19820402
JP	57183788			Α	19821112	JP 1982-56480		19820402
ES	511124		,	A1	19830616	ES 1982-511124		19820402
HU	28787			A2	19831228	HU 1982-1026		19820402
HU	191353			В	19870227			
SU	1155157			<b>A3</b>	19850507	SU 1982-3417550		19820402
PRIORITY	APPLN.	INFO.	:			US 1981-246334	Α	19810403
					•	US 1981-246335	Α	19810403
						US 1981-331045	Α	19811216
						EP 1982-301738	Α	19820401

OTHER SOURCE(S):

MARPAT 98:71916

GI

AB Benzothiophenes I [R = H; R1 = COC6H4O(CH2)2NR2R3-4; R2 = R3 = alkyl; R2R3 = (CH2)4-6, (CH2)2O(CH2)2, etc.] were prepared by Friedel-Crafts acylation of I

(R = Ac, Bz, MeSO2; R1 = H) followed by hydrolysis of the ester groups. Thus, HSC6H4OMe-3 was treated with BrCH2COC6H4OMe-4 to give 3-MeOC6H4SCH2COC6H4OMe-4, which was cyclized with polyphosphoric acid to give I (R = Me, R1 = H). Demethylation of the latter followed by esterification with MeSO2Cl gave I (R = MeSO2, R1 = H; II). Friedel-Crafts acylation of 4 g II with 4-Me2N(CH2)2OC6H4COCl gave 6.2 g I [R = MeSO2, R1 = COC6H4O(CH2)2NMe2-4, III]. Hydrolysis of III gave I (R = H). I are estrogens, antiestrogens, and antiandrogens (no data).

=> file reg SINCE FILE COST IN U.S. DOLLARS TOTAL ENTRY SESSION FULL ESTIMATED COST 115.67 124.13 SINCE FILE TOTAL DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SESSION ENTRY CA SUBSCRIBER PRICE -30.42 -30.42

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http://www.cas.org/support/stngen/stndoc/properties.html

=> s e4

L4

1 "RALOXIFENE HYDROCHLORIDE"/CN

=> d l4 1 ide

- L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
- RN 82640-04-8 REGISTRY
- ED Entered STN: 16 Nov 1984
- CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl] [4-[2-(1-piperidinyl)ethoxy]phenyl]-, hydrochloride (1:1) (CA INDEX NAME)
  OTHER CA INDEX NAMES:
- CN Methanone, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]-, hydrochloride (9CI)
  OTHER NAMES:

CN Bonebay

CN Bontact

CN Evista

CN Fiona

CN Keoxifene hydrochloride

CN LY 156758

CN Ralofen

CN Raloxifene hydrochloride

CN Reloxafine

MF C28 H27 N O4 S . Cl H

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CIN, CSCHEM, EMBASE, HSDB\*, IMSPATENTS, IMSRESEARCH, IPA, MRCK\*, MSDS-OHS, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL (\*File contains numerically searchable property data)

CRN (84449-90-1)

HCl

#### \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

329 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
329 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file caplus COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 8.25 132.38 SINCE FILE TOTAL DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -30.42

FILE 'CAPLUS' ENTERED AT 13:35:36 ON 21 AUG 2007
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FILE COVERS 1907 - 21 Aug 2007 VOL 147 ISS 9 FILE LAST UPDATED: 20 Aug 2007 (20070820/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

## http://www.cas.org/infopolicy.html

=> s 14

L5 329 L4

. => d scan

- L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
- CC 63-6 (Pharmaceuticals)
- TI Preparation of raloxifene hydrochloride capsules and establishment of its quality control standard
- ST raloxifene hydrochloride capsules dissoln quality control
- IT Drug delivery systems

(capsules; preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

IT Dissolution

Quality control

(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

IT 63-42-3, Lactose 9004-32-4, Carboxymethyl cellulose sodium 9004-34-6, Cellulose, biological studies

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(preparation of raloxifene hydrochloride capsules and establishment of

(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

IT 82640-04-8, Raloxifene hydrochloride

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of raloxifene hydrochloride capsules and establishment of quality control standard)

#### HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

- L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
- CC 2-4 (Mammalian Hormones)

Section cross-reference(s): 1

- TI Effectiveness of combined GnRH analogue plus raloxifene administration in the treatment of uterine leiomyomas: a prospective, randomized, single-blind, placebo-controlled clinical trial
- ST leuprolide acetate SERM raloxifene pelvic pain menorrhagia uterine leiomyomas
- IT Human

(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Intestine, disease

(constipation; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine

leiomyomas)

IT Menopause

(hot flash; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Uterus, neoplasm

(leiomyoma; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Menstrual disorder

(menorrhagia; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Body, anatomical

(pelvis, pain; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Menopause

(premenopause; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Estrogen receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (selective modulator of; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT Urinary system, disease

(urinary frequency; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT 74381-53-6, Leuprolide acetate

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Enantone; GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

IT 82640-04-8, Raloxifene hydrochloride

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(GnRH analog (Enantone) plus raloxifene hydrochloride (Evista) effectiveness in treatment of premenopausal women with uterine leiomyomas)

#### HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

- L5 329 ANSWERS CAPLUS COPYRIGHT 2007 ACS on STN
- IC ICM C07D333-64

ICS C07D333-56

- CC 27-9 (Heterocyclic Compounds (One Hetero Atom))
- TI Demethylation process for preparing benzo[b]thiophenes
- ST demethylation benzothiophene benzenethiol
- IT 63675-73-0P 63675-74-1P 84541-36-6P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (demethylation process for preparing benzo[b]thiophenes)

IT 63676-25-5P 82640-04-8P 84449-87-6P 84449-90-1P

215662-11-6P 215662-12-7P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(demethylation process for preparing benzo[b]thiophenes)

```
ΙT
     108-90-7, Chlorobenzene, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (demethylation process for preparing benzo[b]thiophenes)
ΙT
                7340-90-1 7446-70-0, Aluminum chloride, reactions
     15570-12-4, 3-Methoxybenzenethiol
                                         84449-80-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (demethylation process for preparing benzo[b]thiophenes)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
L5
      329 ANSWERS
                    CAPLUS COPYRIGHT 2007 ACS on STN
IC
     ICM A61K031-445
     ICS A61K031-40; A61K031-38
INCL 514324000
     63-6 (Pharmaceuticals)
CC
     Section cross-reference(s): 1
TI
     Methods of decreasing serum calcium levels
     benzoyl benzothiophene calcium blood decrease; raloxifene calcium blood
ST
     decrease-
IT
     82640-04-8, Raloxifene hydrochloride
                                            84449-90-1, Raloxifene
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (benzoylbenzothiophene derivs. for decreasing serum calcium levels)
     7440-70-2, Calcium, biological studies
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (benzoylbenzothiophene derivs. for decreasing serum calcium levels)
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1
                    CAPLUS COPYRIGHT 2007 ACS on STN
L5
      329 ANSWERS
     C12Q001-02
IC
INCL 435029000
     2-1 (Mammalian Hormones)
CC
     Cell culture for screening estrogen agonists and antagonists
TI
     estrogen agonist screening cell culture; antagonist estrogen screening
ST
     cell culture
     Animal cell line
IT
        (C7 MCF7-173, in screening of estrogen agonists/antagonists)
IT
     Estrogens
     RL: ANST (Analytical study)
        (agonists, cell culture method for screening of)
     Cell proliferation
IT
        (cells dependent on estrogens for, in screening of estrogen
        agonists/antagonists)
IT
     Charcoal
     RL: ANST (Analytical study)
        (dextran-, human serum stripped with, for maintaining medium in cell
        culture method for screening of estrogen agonists/antagonists)
IT
    Blood serum
        (fetal bovine, for maintaining medium in cell culture method for
        screening of estrogen agonists/antagonists)
IT
     Animal tissue culture
        (for estrogen agonist/antagonist screening)
     Proteins, biological studies
IT
     RL: BIOL (Biological study)
        (inhibitory to proliferation of estrogen-dependent cells in vitro, for
        cell culture method for screeing of estrogen agonists/antagonists)
    Estrogens
IT
```

RL: PRP (Properties)

(antiestrogens, cell culture method for screening of)

IT Mammary gland

(neoplasm, cells of, in screening of estrogen agonists/antagonists)

RL: ANST (Analytical study)

(agonists and antagonists of, cell culture method for screening of)

IT 9004-54-0, Dextran, biological studies

RL: BIOL (Biological study)

(charcoal-, human serum stripped with, for maintaining medium in cell culture method for screening of estrogen agonists/antagonists)

IT 10540-29-1, Tamoxifen 34816-55-2, Moxestrol 63676-25-5, LY117018 71794-60-0, 11β-Chloromethylestradiol 82640-04-8, LY156758

120382-04-9, RU39411 57-83-0, Progesterone, biological studies

RL: ANST (Analytical study)

(estrogen agonist/antagonist activity of, determination of, cell culture method

for)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s 14/prep

329 L4

4449106 PREP/RL

L6 34 L4/PREP

(L4 (L) PREP/RL)

=> d 16 ibib abs 1-

YOU HAVE REQUESTED DATA FROM 34 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2007:265820 CAPLUS Full-text

DOCUMENT NUMBER:

146:448285

TITLE:

Benzothiophenes, formulations containing same, and

methods

INVENTOR(S):

Cullinan, George J.; Palkowitz, Alan D.

PATENT ASSIGNEE(S):

USA

SOURCE:

Hung. Pat. Appl., 40pp.

CODEN: HUXXCV

DOCUMENT TYPE:

Patent

LANGUAGE:

Hungarian

FAMILY ACC. NUM. COUNT:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
,				
HU 9901882	A2	20000228	HU 1999-1882	19970219
HU 9901882	A3	20000328		
PRIORITY APPLN. INFO.:			HU 1999-1882	19970219
OTHER SOURCE(S):	MARPAT	146:448285		•
GI				

$$\begin{array}{c|c}
 & \text{OCH}_2\text{CH}_2\overset{\text{O}}{\text{N}} = \mathbb{R}^3 \\
 & \text{R4}
\end{array}$$

AB Benzothiophene N-oxides I [R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, C1 or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

L6 ANSWER 2 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2006:958171 CAPLUS Full-text

DOCUMENT NUMBER:

147:9760

TITLE:

Synthesis of raloxifene hydrochloride

AUTHOR (S):

Song, Yan-ling; Zhao, Yan-fang; Meng, Yan-qiu; Gong,

Pina

CORPORATE SOURCE:

Shenyang Institute of Chemical Technology, Faculty of

Pharmaceutical-Engineering, Shenyang, 110142, Peop.

Rep. China

SOURCE:

Zhongguo Xinyao Zazhi (2005), 14(7), 882-884

CODEN: ZXZHA6; ISSN: 1003-3734

PUBLISHER:

Zhongguo Xinyao Zazhi Youxian Gongsi

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

The synthesis of raloxifene hydrochloride [i.e., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride] is reported. The target compound was synthesized from 3-methoxybenzenethiol and 4-methoxy-α-bromo acetophenone via five steps, including substitution, cyclization, Friedel-Crafts reaction, di-Me reaction and salt formation. The structure of the target compound was confirmed by IR, 1H-NMR and MS. This synthetic route required mild conditions and provided an improved yield and was easily controlled.

L6 ANSWER 3 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:1257978 CAPLUS Full-text

DOCUMENT NUMBER:

144:135192

TITLE:

Manufacture of raloxifene-hydrochloride-containing medicines for treating bone fracture delayed union or

nonunion

INVENTOR(S):

Zhang, Jianhao; Huang, Haibo

PATENT ASSIGNEE(S):

Peop. Rep. China

SOURCE:

Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp...

CODEN: CNXXEV

DOCUMENT TYPE:

Patent Chinese

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. PATENT NO. KIND DATE DATE ----CN 1615860 Α 20050518 CN 2003-10113253 20031111 PRIORITY APPLN. INFO.: CN 2003-10113253 20031111

The title medicines are manufd. from (by wt.) raloxifene hydrochloride (35-45%) as effective components, diluent (50-60%), disintegrant (2-4%), lubricant (0.5-1%), and adhesive (2-3%). The medicines can be produced into various drug forms such as tablets, capsules, suspensions, powders, granules, solns., etc., and have advantages of short course of treatment, high recovery rate, etc.

ANSWER 4 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:547361 CAPLUS Full-text

DOCUMENT NUMBER:

143:59836

TITLE:

A process for preparing benzoic acid derivatives,

useful as intermediates for preparation of raloxifene

INVENTOR(S):

Luke, Wayne Douglas

PATENT ASSIGNEE (S):

Eli Lilly and Company, USA

U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
				~~~~~
US 2005137396	A1	20050623	US 2003-745188	20031222
US 7012153	B2	20060314		
PRIORITY APPLN. INFO.:		•	US 2003-745188	20031222

CASREACT 143:59836; MARPAT 143:59836

The invention relates to a prepn. of benzoic acid derivs. of formula RO2C-p-C6H4-O(CH2)2-3N(R1)R2 [wherein: R is alkyl; R1 and R2 are independently alkyl, or combined together with the nitrogen atom form piperidinyl, pyrrolidinyl, or morpholinyl, etc.], useful as intermediates for preparation of raloxifene. For instance, 4-[2-(piperidin-1- yl)ethoxy]benzoic acid hydrochloride was prepared via etherification of Me 4-hydroxybenzoate by 1-( $\beta$ chloroethyl)piperidine hydrochloride and subsequet hydrolysis with a yield of 99.2%.

REFERENCE COUNT:

9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2005:29327 CAPLUS Full-text

DOCUMENT NUMBER:

142:134465

TITLE:

Process for preparing raloxifene hydrochloride

INVENTOR(S):

Ferrari, Massimo; Zinetti, Fabrizio; Belotti, Paolo

PATENT ASSIGNEE(S):

Erregierre S.p.A., Italy

PCT Int. Appl., 19 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

#### PATENT INFORMATION:

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PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
                                            ______
                         _ _ _ _
                         A1
                                20050113
                                            WO 2004-EP51263
                                                                   20040628
     WO 2005003116
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     CA 2549354
                          A1
                                20050113
                                            CA 2004-2549354
                                                                   20040628
                                            EP 2004-741907
     EP 1641773
                          A1
                                20060405
                                                                   20040628
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
     US 2007100147
                          A1
                                20070503
                                            US 2005-562762
                                                                   20051227
PRIORITY APPLN. INFO.:
                                            IT 2003-MI1333
                                                                A 20030630
                                            WO 2004-EP51263
                                                                W 20040628
```

OTHER SOURCE(S): CASREACT 142:134465

A process for prepg. raloxifene hydrochloride with a purity greater than 98% and low aluminum content comprises the following stages : (a) demethylation of 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene in pyridine and hydrochloric acid to obtain 6-hydroxy-2-(4- hydroxyphenyl)benzo[b]thiophene in pyridine hydrochloride, (b) acetylation of 6-hydroxy-2-(4hydroxyphonyl)benzo[b]thiophene with an acetylating agent to obtain the corresponding 6-acetoxy-2-(4- acetoxyphenyl)benzo[b]thiophene (I), (c) acylation of 6-acetoxy-2-(4- acetoxyphonyl)benzo[b]thiophene with 4-(2piperidinoethoxy) benzoylchloride hydrochloride with aluminum trichloride in a halogenated solvent to obtain 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2piperidinoethoxy)benzoyl] - benzo[b]thiophene, (d) hydrolysis of 6-acetoxy-2-(4-acetoxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thiophene according to the following operating conditions: (d1) treatment of 6-acetoxy-2-(4-acetoxyphonyl)-3-[4- (2-piperidinoethoxy)benzoyl]benzo[b]thiophene with alkaline hydroxide in alc. solvent, (d2) acidification of the product obtained in the preceding stage (d1) with a strong acid, to obtain the corresponding raloxifene salt with the strong acid, characterized in that the strong acid used in stage (d2) is concentrated hydrochloric acid. Thus, thionyl chloride was added to a mixture of 4-(2-piperidinoethoxy) benzoic acid HCl salt and pyridine in refluxing methylene chloride; the mixture was stirred for 1 h and the solvent was distilled off; the mixture was cooled to 20°C, and I was The resulting mixture was mixed with aluminum trichloride in methylene chloride at 15°C to 30°C; the mixture was stirred for 1 h and was worked up : the product was treated with sodium hydroxide in methanol; water, Et acetate, and HCl were added; the suspension was centrifuged to give crude raloxifene hydrochloride.

REFERENCE COUNT:

2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 2004:617920 CAPLUS Full-text

DOCUMENT NUMBER: 142:463529

TITLE: Synthesis of raloxifene hydrochloride AUTHOR(S): Gong, Ping; Zhao, Yanfang; Wang, Dun

CORPORATE SOURCE: School of Pharmaceutical Engineering, Shenyang
Pharmaceutical University, Shenyang, 110016, Peop.

Rep. China

SOURCE:

Shenyang Yaoke Daxue Xuebao (2003), 20(2), 111-113

CODEN: SYDXFF; ISSN: 1006-2858

PUBLISHER:

Shenyang Yaoke Daxue Xuebao Bianjibu

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

OTHER SOURCE(S):

CASREACT 142:463529

Raloxifene hydrochloride, which is a selective estrogen receptor modulator, was synthesized from 3-methoxybenzenethiol and 2-bromo- 4'-methoxyacetophenone by etherification, cyclization in the presence of polyphosphoric acid, hydrolysis with HBr/HOAc to obtain 6-hydroxy- 2-(4-

hydroxyphenyl) benzothiophene, acylation with acetic anhydride, acylation with 4-[2-(1-piperidinyl)ethoxy]benzoyl chloride in the presence of AlCl3,

saponification with 5M NaOH solution in methanol, and saltification with HCl. The overall yield was 10.0%, and its structure was confirmed by MS, 1H NMR,

13C NMR.

ANSWER 7 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

2002:348716 CAPLUS Full-text

DOCUMENT NUMBER:

138:137104

TITLE:

Synthesis of Raloxifene hydrochloride as selective

estrogen receptor modulator

AUTHOR(S):

Chen, Yanzhong; Liu, Yingxiang

CORPORATE SOURCE:

Guangdong College of Pharmacy, Canton, 510224, Peop.

Rep. China

SOURCE:

Guangdong Yaoxueyuan Xuebao (2002), 18(1), 1-3, 20

CODEN: GYXUF8

PUBLISHER:

Guangdong Yaoxueyuan

DOCUMENT TYPE:

Journal

LANGUAGE:

Chinese

OTHER SOURCE(S):

CASREACT 138:137104

Raloxifene was synthesized from α-bromo-p-methoxyacetophenone and mmethoxybenzenethiol via condensation, cyclization, acylation, and demethylation with the overall yield 49.2%. The chemical structure of compound was confirmed by 1H NMR, MS, IR, and elementary anal. The reaction conditions were mild and starting materials were com. available.

ANSWER 8 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN L6

ACCESSION NUMBER:

2001:247325 CAPLUS Full-text

DOCUMENT NUMBER:

134:266100

TITLE:

Synthesis of 4-[(2-piperidin-1-yl)ethoxy]benzoic acid

for manufacture of Raloxifene hydrochloride

INVENTOR(S):

Luke, Wayne Douglas

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

SOURCE: ·

PCT Int. Appl., 32 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

English

PATENT NO. KIND					<b>D</b> 1	DATE		APPLICATION NO.						DATE			
					-				<del>-</del>					-			
WO 2001	0233	69		A2	:	2001	0405	,	WO 2	000-	US21	974	,	2	0000	918	
W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	
	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	
	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,	RU,	

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1220847 A2 20020710 EP 2000-966691 20000918

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003510313 T 20030318 JP 2001-526522 20000918

PRIORITY APPLN. INFO.: US 1999-156205P

WO 2000-US21974 W 20000918

P

19990927

OTHER SOURCE(S): CASREACT 134:266100; MARPAT 134:266100

AB An improved process for the prepn. of 4[(2-piperidin-1-yl)ethoxy]benzoic acid derivs. comprises reacting haloalkyl amine X(CH2)nNR1R2 (X = halogen; R1, R2 = C1-4 alkyl, combined with nitrogen atom to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, 1-hexamethyleneimino group; n = 2, 3) with C1-6 alkyl p-hydroxybenzoate in the presence of a hydrated inorg. base in an appropriate solvent.

L6 ANSWER 9 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1999:12339 CAPLUS Full-text

DOCUMENT NUMBER:

130:66385

TITLE:

Process for preparing benzoic acid derivatives as

intermediates in the synthesis of benzothiophenes

INVENTOR(S):

Chelius, Erik Christopher Eli Lilly and Company, USA

PATENT ASSIGNEE(S):

U.S., 7 pp.

SOURCE:

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1. 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5852193	A	19981222	US 1998-69277		19980429
US 6075146	Α	20000613	US 1998-123889		19980728
PRIORITY APPLN. INFO.:		•	US 1997-45162P	P	19970430
			US 1998-69277	A3	19980429
OTHER SOURCE(S):	ÇASRE	ACT 130:66385	; MARPAT 130:66385		

# \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compds. [I; R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; R6 = carboxy protecting group] were prepared by reacting a hydroxylamine HO(CH2)nNR1R2 with a compound selected from W2O and W-halo (wherein W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.) followed by reaction of the resulting Y1(CH2)nNR1R2 (Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, etc.) with a compound II. Compds. I can be then reacted with benzothiophenes III (R4, R5 = hydroxy protecting groups) to afford compds. IV (R4, R5 = , H, hydroxy protecting groups) (example of such reaction was given).

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:721690 CAPLUS Full-text

DOCUMENT NUMBER: 130:3769

TITLE: Processes for preparing benzothiophenes

INVENTOR(S): McGill, John McNeil, III; Misner, Jerry Wayne; Zhang,

Tony Yantao

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE: English

PATENT INFORMATION:

FAMILY ACC. NUM. COUNT:

											LICAT			D	ATE	
											1998-			 1	9980	428
•											, CA,					
											, KP,					
			-		-						, NZ,					
		-									, UZ,			·	·	•
	RW:	•	•	•	•		•				, BF,			CI,	CM,	GA,
							TD,		•			•	•			
CA	2287	943	·		A1		1998	1105		CA	1998-	2287	943	1	9980	428
AU	9872	613			Α		1998	1124		AU	1998-	7261	3	1	9980	428
BR	9809	439			Α		2000	0613		BR	1998-	9439		1	9980	
HU	2000	0318	7		A2		2001	0528		HU	2000-	3187	•	1	9980	428
											1998-				9980	
											1998-				9980	429
											1998-					
											, IT,					
							RO							•		
MX	9909	883			Α		2000	0331		MX	1999-	9883		1	9991	027
PRIORITY	APP	LN.	INFO	. :						US	1997-	4517	7P	P 1	9970	430
											1998-					
OTHER SO	OURCE	(S):			CASI	REAC	T 13	0:37	69;	MAR	PAT 1	30:3	769			
GI																

## \* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compds. [I; Y = Cl, Br, I, SO2(Cl-4 alkyl), etc.] were prepd. by reacting benzo[b]thiophene II [R51, R52 = hydroxy protecting groups] with benzoyl chloride III [R8 = acyl activating group] in the presence of a boron trihalide such as BCl3. Compds. I were reacted further with an amine HNR6R7 [R6, R7 = Cl-4 alkyl; NR6R7 = piperidino, pyrrolidino, morpholino, etc.] to produce benzothiophenes IV and their salts.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:721501 CAPLUS Full-text

DOCUMENT NUMBER: 13

130:3768

OCOMENI NOMBER: 130:376

TITLE: Demethylation process for preparing benzo[b]thiophenes

INVENTOR(S): . Hoard, David Warren; Luke, Wayne Douglas

PATENT ASSIGNEE(S): Eli Lilly and Company, USA SOURCE: Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 875511	A1	19981104	EP 1998-303345	19980429
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IT, LI, LU, NL,	SE, MC', PT,
IE, SI, LT,	LV, FI	, RO		
CA 2236254	A1	19981030	CA 1998-2236254	19980427
JP 11005789	Α	19990112	JP 1998-118628	19980428
US 5994547	Α	19991130	US 1998-69500	19980429
PRIORITY APPLN. INFO.:		•	US 1997-45156P	P 19970430
OTHER SOURCE(S):	CASREA	CT 130:3768;	MARPAT 130:3768	
GI				

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The prepn. of benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, AB pyrrolidino, etc.] by the acylation of alkoxy protected starting materials followed by demethylation of II using essentially odorless thiol compound (2methyl-5-t-Bu-benzenethiol) are provided herewith. Demethylation may be carried out in the same reaction vessel without isolation of the acylated, protected material.

REFERENCE COUNT:

10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2007 ACS on STN ANSWER 12 OF 34 L6 1998:721498 CAPLUS Full-text

ACCESSION NUMBER: DOCUMENT NUMBER:

130:3767

TITLE:

Process for preparing benzoic acid derivative

intermediates and benzothiophene pharmaceuticals

INVENTOR (S):

Chelius, Erik Christopher

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA

Eur. Pat. Appl., 16 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

#### PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
EP 875507	A1 19981104	EP 1998-303340	19980429
R: AT, BE, CH,	DE, DK, ES, FR, GB,	, GR, IT, LI, LU, NL,	SE, MC, PT,
IE, SI, LT,			
CA 2231013	A1 19981030	CA 1998-2231013	19980304
JP 10316674	A 19981202	JP 1998-116564	19980427
PRIORITY APPLN. INFO.:		US 1997-45162P	P 19970430
OTHER SOURCE(S):	CASREACT 130:3767;	MARPAT 130:3767	
GI	•		

The novel intermediates Y1(CH2)nNR1R2 [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2-3; Y1 = p-toluenesulfonyloxy, methylsulfonyloxy, trifluoromethylsulfonyloxy, 2,2,2-trifluoroethylsulfonyloxy, trifluoroacetoxy], useful as intermediates in synthesis of benzothiophenes I and their salts, were prepared by reaction a hydroxylamine HO(CH2)nNR1R2 with W2O and W(halo) [W = p-toluenesulfonyl, methylsulfonyl, trifluoromethylsulfonyl, etc.].

REFERENCE COUNT:

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

19

ACCESSION NUMBER:

1998:719256 CAPLUS Full-text

DOCUMENT NUMBER:

130:3764

TITLE:

A regioselective alkylation process for preparing

substituted benzo[b]thiophenes

INVENTOR(S):

McGill, John McNeil, III; Miller, Randal Scot

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

	CENT 1				KIN		DATE		2	APPL	ICAT:	ION 1	NO.		D	ATE	
						_	-,								-		
WO	9848	792			A1		1998	1105	1	WO 1	998-1	JS84	77		1:	99804	128
	W:	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
		DK,	EE,	ES,	FI,	GB,	GE,	GH,	GM,	GW,	HU,	ID,	IL,	IS,	JP,	KE,	KG,
		KP,	KR,	ΚŻ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
		NO,	NZ,	PL,	ΡŤ,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TR,	TT,
		UA,	UG,	US,	UΖ,	VN,	YU,	ZW,	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM
	RW:	GH.	GM.	KE.	LS.	MW.	SD.	SZ.	UG.	ZW.	AT.	BE.	CH.	CY.	DE.	DK.	ES.

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 1998-2287918 19980428 CA 2287918 **A1** 19981105 AU 1998-71653 19980428 AU 9871653 Α 19981124 EP 979075 20000216 EP 1998-918798 19980428 A1 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI JP 2001523252 T · 20011120 JP 1998-547259 19980428 19980429 20000215 US 1998-69276 US 6025495 Α PRIORITY APPLN. INFO.: US 1997-45132P 19970430 WO 1998-US8477 . 19980428 CASREACT 130:3764; MARPAT 130:3764 OTHER SOURCE(S):

$$0 \longrightarrow 0 \longrightarrow 0 \xrightarrow{R^1} N_{R^2}$$

AB The title benzo[b]thiophenes I [R1, R2 = C1-4 alkyl; NR1R2 = piperidino, pyrrolidino, morpholino, etc.; n = 2, 3] such as raloxifene, were prepared by the regioselective alkylation of benzothiophene II with Y(CH2)nNR1R2 [Y = C1, p-TsO] in the presence of a suitable base.

REFERENCE COUNT:

6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1998:192131 CAPLUS Full-text

DOCUMENT NUMBER:

128:275070

TITLE:

GI

Benzothiophenes, formulations containing same, and

methods

INVENTOR(S):

Cullinan, George Joseph; Palkowitz, Alan David

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE:

U.S., 10 pp.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE

APPLICATION NO.

DATE

US 5731342 A 19980324 US 1997-787041 19970127

PRIORITY APPLN. INFO.: OTHER SOURCE(S):

MARPAT 128:275070

GI

$$X \longrightarrow OCH_2CH_2NR^3R^4$$
 $R^2$ 

Benzothiophene N-oxides [I; R1 = H, OH, alkoxy, OCO2(alkyl or aryl), OCO(alkyl or aryl), etc.; R2 = R1, Cl or F; R3 and R4 = alkyl or combine to form polymethylene or morpholine; X = CH2, CHOH, O or CO], useful for the treatment or prevention of medical indications associated with post-menopausal syndrome and breast cancer, are prepared Thus, [2-(4-hydroxyphenyl)-6-hydroxybenzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone was oxidized using 30% aqueous H2O2 to give I [R1 = R2 = OH, R3R4 = (CH2)5, X = CO]. I reduce serum cholesterol compared to ovariectomized rats and do not cause a large increase in the number of eosinophils observed in the stromal layer of the ovariectomized rat uteri. In an osteoporosis test, I prevent bone loss in a general, dose-dependent manner. I were active in the MCF-7 proliferation assay and inhibited growth of DMBA-induced mammary tumors. A tablet formulation comprises: I 2.5-1000, cellulose 200-650, silicon dioxide 10-650, and stearic acid 5-15 mg/tablet.

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

US 1997-787041

19970127

L6 ANSWER 15 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

5

ACCESSION NUMBER:

1998:161136 CAPLUS Full-text

DOCUMENT NUMBER:

128:221639

TITLE:

Preparation of amorphous benzothiophenes for

pharmaceuticals

INVENTOR(S):

Cuff, George W.; Thakkar, Arvind L.

PATENT ASSIGNEE(S):

Eli Lilly and Company, USA; Cuff, George W.; Thakkar,

Arvind L.

SOURCE:

PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PAT	CENT I	NO.			KIN	D :	DATE		i	APPL	ICAT:	ION 1	10.		D	ATE	
						-											
WO	98089	513			<b>A1</b>		1998	0305	. 1	WO 1	997-1	US14'	768		19	99708	822
	W: ·	AL,	AM,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CN,	CU,	CZ,	EE,	GE,	GH,
	-	HU,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LT,	LV,	MD,	MG,
		MK,	MN,	MW,	MX,	NO,	NZ,	PL,	RO,	RU,	SD,	SG,	SI,	SK,	SL,	ТJ,	TM,
		TR,	TT,	UA,	UG,	US,	UZ,	VN,	ΥU,	ZW							
	RW:	GH,	KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,

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ML, MR, NE, SN, TD, TG
                               19980304
                                          EP 1997-306426
                                                                 19970822
    EP 826682
                         A1
    EP 826682
                         В1
                               20030312
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
    CA 2263175
                         A1
                               19980305
                                           CA 1997-2263175
                                                                 19970822
    AU 9742335
                         Α
                               19980319
                                           AU 1997-42335
                                                                 19970822
    AU 723987
                         B2
                               20000907
                                           IN 1997-CA1549
                                                                 19970822
    IN 182940
                         A1
                               19990814
                                          BR 1997-13176
                                                                 19970822
    BR 9713176
                         Α
                               20000208
    CN 1244124
                                           CN 1997-197434
                                                                 19970822
                         Α
                               20000209
                                           HU 2000-1172
                                                                 19970822
    HU 200001172
                         A2
                               20010628
    HU 200001172
                        A3
                               20020128
                                                                 19970822
    NZ 333839
                         Α
                               20010629
                                          NZ 1997-333839
    IL 128641
                        Α
                               20011031
                                           IL 1997-128641
                                                                 19970822
                               20020121
                                          TR 1999-403
    TR 9900403
                       T2
                                                                 19970822
                                          JP 1998-511744
    JP 2002514174
                        Т
                               20020514
                                                                 19970822
                                          AT 1997-306426
                         Т
    AT 234295
                               20030315
                                                                 19970822
                                           ES 1997-306426
    ES 2195089
                         Т3
                               20031201
                                                                 19970822
                               19990225
                                           ZA 1997-7617
                                                                 19970825
    ZA 9707617
                         Α
                         B1
                                          US 1997-918741
                                                                 19970825
    US 6713494
                               20040330
                               19990225
                                          NO 1999-914
    NO 9900914
                         Α
                                                                 19990225
                       . . A
                                           KR 1999-701682
                                                                . 19990227
    KR 2000035941
                               20000626
                                                              P 19960828
PRIORITY APPLN. INFO.:
                                           US 1996-24831P
                                                              W 19970822
                                           WO 1997-US14768
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OTHER SOURCE(S): MARPAT 128:221639

AB A method for prepg. an amorphous form of a benzothiophene such as raloxifene is described. Thus, raloxifene-HCl was prepared by a series of reactions starting from 3-methoxybenzenethiol and 4'-methoxyphenacyl bromide. A formulation contained PEG-1450 70, spray-dried lactose 1.5, colloidal SiO2 1.5, Polysorbate-80 2.0, and raloxifene-HCl 25%. The bioavailability of raloxifene-HCl and the pharmacol. effects of this compound on osteoporosis and hyperlipidemia were determined

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1997:640660 CAPLUS Full-text

1

DOCUMENT NUMBER:

127:307297

TITLE:

Preparation of 3-[4-(2-aminoethoxy)benzoyl]-2-aryl-6- ~

hydroxybenzo[b]thiophenes.

INVENTOR(S):

Jones, Charles David; McGill, John McNeill, III

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA; Jones, Charles David; McGill,

John McNeill, III

SOURCE:

PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

1

FAMILY ACC. NUM. COUNT:

PAT	rent 1	NO.		•	KIN	<b>o</b> :	DATE		;	APPL	ICAT:	ION I	. 00		D	ATE	
						-									-		
WO	9734	888			A1		1997	0925	1	WO 1	996-1	US39:	34		1:	9960:	320
	W:	AL,	AM,	AT,	AU,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,	ES,
		FI,	GB,	GE,	HU,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LK,	LR,	LS,	LT,	LU,
		LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,
		SI,	SK,	TJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,	AM,	AZ,	BY,	KG,	KZ,
		MD,	RU,	TJ,	TM												
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IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 2249406 **A1** 19970925 CA 1996-2249406 19960320 AU 9652586 Α 19971010 AU 1996-52586 19960320 EP 888331 19990107 EP 1996-908892 19960320 **A1** AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI JP 2000506885 Т 20000606 JP 1997-533424 19960320 19980821 US 6008377 Α 19991228 US 1998-125848 US 1996-13674P PRIORITY APPLN. INFO.: 19960319 WO 1996-US3934 19960320 W

OTHER SOURCE(S):

CASREACT 127:307297; MARPAT 127:307297

GI

AB Title compds. (I; R1 = H, OH; R2, R3 = alkyl; R2R3N = pyrrolidino, piperidino, hexamethyleneimino, morpholino; HX = HCl, HBr) were prepared by reaction of PhOCH2CH2NR2R3.HX (variables as above) with acyl derivative (II; R4 = H, alkoxy; R5 = alkyl; R6 = C1, Br, OH) in the presence of BX3. Thus, 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene-3-carbonyl chloride (preparation given), and Ph 2-N-piperidinylethyl ether hydrochloride (preparation given) in 1,2dichloroethane at 0° were treated with BCl3 in 1,2-dichloroethane at 0° followed by warming to 35° for 16-20 h to give 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2- piperidinoethoxy) benzoyl] benzo[b] thiophene hydrochloride 1,2dichloroethane solvate.

CAPLUS COPYRIGHT 2007 ACS on STN ANSWER 17 OF 34 ACCESSION NUMBER: 1997:124441 CAPLUS Full-text

DOCUMENT NUMBER:

126:143973

TITLE:

Diaryl vinyl sulfoxides, a process for their synthesis, and their use in the preparation of

INVENTOR(S):

benzothiophene derivatives Aikins, James A.; Miller, Randal S.; Zhang, Tony Y.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA; Aikins, James A.; Miller,

Randal S.; Zhang, Tony Y.

SOURCE:

PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.

KIND DATE APPLICATION NO.

DATE

WO 9640691	A1 19961219	WO 1996-US9163	19960604
W: AL, AM, A	r, Au, Az; BB, BG,	BR, BY, CA, CH, CN, CZ	, DE, DK, EE,
ES, FI, G	B, GE, HU, IL, IS,	JP, KE, KG, KP, KR, KZ,	, LK, LR, LS,
LT, LU, L	, MD, MG, MK, MN,	MW, MX, NO, NZ, PL, PT,	, RO, RU, SD,
SE, SG			•
RW: KE, LS, M	N, SD, SZ, UG, AT,	BE, CH, DE, DK, ES, FI	, FR, GB, GR,
IE, IT, L	J, MC, NL, PT, SE,	BF, BJ, CF, CG, CI, CM	
		US 1995-478706	
US 6372945	B1 20020416	US 1995-483130	19950607
CA 2220145	A1 19961219	CA 1996-2220145	19960604
AU 9660920	A 19961230	AU 1996-60920	19960604
AU 697352	B2 · 19981001		
		EP 1996-918211	19960604
R: AT, BE, C	H, DE, DK, ES, FR,	GB, GR, IT, LI, LU, NL,	, SE, PT, IE,
SI, LT, L	/, FI		
CN 1192741	A 19980909	CN 1996-196167	19960604
BR 9608579 JP 11507061	A 19990105	BR 1996-8579	
		- · · · · · · · · · · · · · · · · · · ·	19960604
HU 9900922	A2 19990728	HU 1999-922	19960604
HU 9900922	A3 20000628		
NZ 337030	A 20001124	NZ 1996-337030	19960604
NZ 337031	A 20010126	NZ 1996-337031	19960604
	A1 20041029		
NO 9705578	A 19971203	NO 1997-5578	19971203
NO 5987	A 19971203	NO 2000-5987	20001127
CN 1341596	A 20020327	CN 2000-130779	20001215
PRIORITY APPLN. INFO.:		US 1995-478706	A 19950607
		US 1995-483130	A 19950607
	•	NZ 1996-310179	A1 19960604
		WO 1996-US9163	
OTHER SOURCE(S):	CASREACT 126:14	3973; MARPAT 126:143973	

 $\mathbb{R}^{1}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{1}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$   $\mathbb{R}^{2}$ 

GI

AΒ

The invention is directed to new diarylvinyl sulfoxides I [R1, R2 = H, alkoxy, arylalkoxy, halo, amino; R3 = thermally labile or acid-labile alkyl, alkenyl,

or arylalkyl group], and to a new process for their synthesis. I are useful precursors for 2-aryl-substituted benzothiophenes II, which are in turn intermediates for the drugs III.HX [R1, R2 = H, halo, amino, OH; R4, R5 = alkyl; or NR4R5 = pyrrolidino, piperidino, hexamethyleneimino, morpholino; X = Cl, Br]. For instance, treatment of 4-MeOC6H4CH2COC6H4OMe-4 with TiCl4 in THF and reaction with Me3CSH and Et3N gave the vinyl sulfide (E)-4-MeOC6H4CH:C(SCMe3)C6H4OMe-4 [(E)-IV]. Alternatively, lithiation of 4-MeOC6H4CH2SCMe3 with BuLi and condensation with 4-MeOC6H4CHO gave (Z)-IV. Oxidation of either isomer of IV with a dilute AcOH solution of peracetic acid, in PhMe at -20°, gave the corresponding sulfoxide I [R1 = R2 = OMe; R3 = CMe3]. Dehydrative cyclization of, e.g., the (E)-sulfoxide, using p-MeC6H4SO3H catalyst under Dean-Stark conditions in PhMe, gave the benzothiophene II [R1 = R2 = OMe]. This was acylated by 4-(2piperidinoethoxy) benzoyl chloride HCl in the presence of BCl3 with concomitant demethylation to give the objective compound III.HCl [R1 = R2 = OH, NR4R5 = piperidino].

L6 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1997:113406 CAPLUS Full-text

DOCUMENT NUMBER: 126:117861

TITLE: Process for the synthesis of benzo(b)thiophenes

INVENTOR(S): Aikins, James A.; Zhang, Tony Y.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Aikins, James A.; Zhang, Tony

Υ.

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PA	CENT						DATE						NO.			ATE	
WO	9640						1996						 67				
	W:	AL,	AM,	ΑT,	AU,	AZ,	BB,	ВG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,
		ES,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LK,	LR,	LS,
		LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,
		SE,	SG														
	RW:	KΕ,	LS,	MW,	SD,	SZ,	ŪĠ,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,
		-	-	-			PT,										
US	5606	076					1997										
CA	2223	096					1996										
	9660						1996			AU 1	.996-	6092	1		1	9960	604
ΑU	7029						1999										
EP	8597	70			. A1		1998	0826		EP 1	.996-	9182	12 .		1	9960	604
EP	8597	70			B1		1999	1208					•				
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	PT,	ΙE,
		SI,	LT,	LV,	FΙ												
	1192						1998			CN 1	.996-	1959	43		1	9960	604
CN	1086	699					2002							•			
	9609						1999									9960	
	1150				T		1999				.997-					9960	
	9900				A2		1999			HU 1	.999-	912	•		1	9960	604
	9900						2000						•				
	2197						2001				006		• •			0060	
	1874				T		1999 2000				.996-					9960	
	2140										.996-					9960	
	8597						2000									9960	
ιΓ	1314	40			A		2000	1031		1 L	.996-	1314	40		Т	9960	604

IL 122378	A	20010319	IL 1996-122378		19960604
NO 9705582	Α	19971203	NO 1997-5582		19971203
GR 3032666	Т3	20000630	GR 2000-400364		20000214
PRIORITY APPLN. INFO.:			US 1995-484536	. A	19950607
			IL 1996-122378	<b>A</b> 3	19960604
			WO 1996-US9167	W	19960604

OTHER SOURCE(S): CASREACT 126:117861; MARPAT 126:117861

AB The present invention is directed to a process for the synthesis of 2-arylbenzo[b]thiophenes. E.g., 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophene was prepared from desoxyanisoin and 2-methyl-2-propanethiol via tert-Bu 4,4'-dimethoxystilbenyl sulfoxide.

L6 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:649600 CAPLUS <u>Full-text</u>

DOCUMENT NUMBER:

125:266032

TITLE:

Phosphorous-containing benzothiophenes, their preparation, their use in treating postmenopausal

syndrome-associated indications and estrogen-dependent

diseases, and pharmaceuticals containing them

INVENTOR (S):

Bryant, Henry U.; Dodge, Jeffrey A.; Nissen, Jeffrey

s.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

Engil

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
EP 729964	A1	19960904	EP 1996-300878	19960209		
EP 729964	B1	20010509				
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IE, IT, LI, LU,	NL, PT, SE		
US 6479517	B1	20021112	US 1995-395944	19950228		
ES 2158242	<b>T</b> 3	20010901	ES 1996-300878	19960209		
CA 2169414	A1	19960829	CA 1996-2169414	19960213		
JP 08259560	Α	19961008	JP 1996-25281	19960213		
US 5998443	A	19991207	US 1997-946842	19971008		
PRIORITY APPLN. INFO.:			US 1995-395944	A 19950228		
OTHER SOURCE(S):	MARPAT	125:266032	•			
GI		•				

Phosphorus-contg. benzothiophene compds. I [R1, R2 = H, OH, halo, OPO(0-alkyl)2, OPO(0-aryl)2, OPO(alkyl)2, OPO(aryl)2, OPO3-2, in which not more than one of R1 and R2 may be H, OH or halo; R3, R4 = CO(CH2)3, CO(CH2)4, alkyl, or R3 and R4 combine to form, with the nitrogen to which they are attached, piperidine, morpholine, pyrrolidine, 3-methylpyrrolidine, 3,3-dimethylpyrrolidine, 3,4-dimethylpyrrolidine, azepine, or pipecoline], and pharmaceutically acceptable salts thereof, are provided which are useful for the treatment of the various medical indications associated with postmenopausal syndrome, as well as estrogen-dependent diseases, including cancer of the breast, uterus and cervix. Also provided are intermediate compds. and processes useful for preparing the pharmaceutically active compds. of the invention, as well as pharmaceutical compns. containing compds. of the invention.

L6 ANSWER 20 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:319150 CAPLUS <u>Full-text</u> DOCUMENT NUMBER: 125:86484

TITLE: Preparation of vinyl sulfenic acid derivatives as

benzo[b]thiophene intermediates

INVENTOR(S): Hoard, David W.; Luke, Wayne D.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 15 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PATENT NO.				KIN	D	DATE APPLICATION NO.														
																10050605					
	US	5512	701			A			L9960430 US 1995-482692												
		2224								CA 1996-2224225											
	WO	9640	693			A1					WO 1996-US9460										
•		W:	ΑL,	AM,	AT,	AU,	AZ,	BB,	BG,	BR,	ВУ	ζ, (	CA,	CH,	CN,	CZ,	DE,	DK,	EE,		
			ES,	FI,	GB,	GE,	.HU,	IL,	IS,	JP,	KE	E, I	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LS,		
			LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX	(, l	NO,	NZ,	PL,	PT,	RO,	RU,	SD,		
			SE,	SG																	
		RW:	KE,	LS,	MW,	SD,	SZ	UG,	ΑT,	BE,	CH	I, I	DΕ,	DK,	ES,	FI,	FR,	GB,	GR,		
								PT,													
	ΑU	9661	003			Α				AU 1996-61003							19960604				
•		6980									•								•		
	ΕP	8303	62			A1		19980325 EF			EP 1996-918314					19960604					
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GF	١, ١	ΙΤ,	LI,	LU,	NL,	SE,	PT,	ΙE,		
			SI,	LT,	LV,	FI						•									
	CN	1192	215			Α		1998	0902		CN	199	96-1	19594	47		1	9960	604		
	CN	1068	883			В		2001	0725												
	BR	9608	847			Α		1999	0608		BR	199	96-8	3847			. 1	9960	604		
	JP	9608 1150	7346			Т		1999	0629		JP	199	97-5	5017	74		1	9960	604		
		9900				A2		1999	0728		HU	199	99-9	923			1	9960	604		
	HU	9900	923					2000													
	ΙL	9900: 1221:	27		•	Α		2001	0520		ΙL	199	96-1	12212	27		1	9960	604		
		9705						1998	0128		NO	199	97-5	5633			1	9971	204		
		1330																0001	212		
PRIOR															92						
															07						
		•									WO	199	96-≀	JS946	60	1	W 1	9960	604		

OTHER SOURCE(S): CASREACT 125:86484; MARPAT 125:86484

AB 4-R1C6H4CH:C(R9)C6H4R2-4 [I; R1,R2 = H, (ar)alkoxy, halo, NH2; R9 = SR4; R4 = OSi(R)3, NR5R6, SR8; R = (ar)alkyl, aryl; R5,R6 = H, (ar)alkyl; NR5R6 =

pyrrolidino, piperidino, etc.; R8 = (ar)alkyl, aryl] were prepared by treating I [R9 = SOR3; R3 = labile alk(en)yl or aryl] with a silylating agent optionally followed by reaction with HNR5R6 or HSR8. Thus, (E)-I (R1 = R2 = OMe)(II; R9 = SOCMe3)(preparation given) was treated with (Me2CSiNH)2CO in PhMe followed by Me2NH, in the same pot, to give I (R1 = R2 = OMe, R9 = SNMe2) as a mixture of (E) - and (Z) -isomers. The latter mixt was treated with TsOH to give 6-methoxy-2-(4-methoxyphenyl)benzo[b]thiophe ne.

ANSWER 21 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

1996:307324 CAPLUS Full-text ACCESSION NUMBER:

124:343103 DOCUMENT NUMBER:

Preparation of unsolvated crystalline TITLE:

> 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2piperidinoethoxy) benzoyl] benzo [b] thiophene

hydrochloride.

Smith Labell, Elizabeth; Luke, Wayne Douglas; McNeill INVENTOR(S):

McGill, John, III; Miller, Randal Scot

Eli Lilly and Co., USA PATENT ASSIGNEE(S):

SOURCE: Ger. Offen., 18 pp.

CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT NO.			APPLICATION NO.	DATE
DE 19534744	A1	19960321	DE 1995-19534744	19950919
US 5629425	A	19970513	US 1994-308325	19940919
IN 1995CA00614	Α	20050304	IN 1995-CA614	19950530
IN 1995CA00615	Α	20050304	IN 1995-CA615	19950530
TW 389760	В	20000511	TW 1995-84105614	19950605
TW 412534	В	20001121	TW 1995-84105613	19950605
US 5731327	Α	19980324	US 1995-467485	19950606
EG 21479	A	20011128	EG 1995-455	19950606
US 6399778	в1	20020604	US 1995-469093	19950606
US 6472531	B1	20021029	US 1995-469961	19950606
ES 2109882	A1	19980116	ES 1995-1774	19950913
ES 2109882	B1	19980816		
ES 2129293	A1	19990601	ES 1995-1775	19950913
ES 2129293	B1	20000116		
NL 1001194	A1	19960319	NL 1995-1001194	19950914
NL 1001194	C2	19970404		
NL 1001196	A1	19960319	NL 1995-1001196	19950914
NL 1001196	C2	19970404		
ZA 9507752	Α	19970314	ZA 1995-7752	19950914
ZA 9507753	A	19970314	ZA 1995-7753	19950914
IL 115315	Α	19990922	IL 1995-115315	19950914
IL 115314	Α	20000229	IL 1995-115314	19950914
IL 125283	Α	20010614	IL 1995-125283	19950914
IN 1995CA01111	Α	20051021	IN 1995-CA1111	19950914
CA 2158399	A1	19960320.	CA 1995-2158399	19950915
CA 2158399	С	20010320		
CA 2158400	A1	19960320	CA 1995-2158400	19950915
CA 2158400	С	20061024		•
DK 9501027	A	19960320	DK 1995-1027	19950915
DK 175903	. B1	20050606		
DK 9501028	Α	19960320	DK 1995-1028	19950915
DK 175897	B1	20050530		

	9503657			Α		1996		NO	1	995-	3657			1	9950	915.
	308107			B1			0724							_		
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	313996			B1		2003		an-	-	005	2212			-	9950	015
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	2293602			A B		1996 1998		GB	1	.995-	1903	2		1	9950	910
	2293602 9531730			A			0404	זות	٦.	995-	2172	^		7	9950	010
	691955			B2		1998		AU		. 993	J I / J	U			9930	910
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	2860071			В2			0224									
	1127253			A		1996	0724	CN	1	995-	1186	29		1	9950	918
	1075069			В			1121									
JP	08193081			Α		1996	0730	JP	1	995-	2382	09		1	9950	918
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BR	9504060			A		1996	0924			.995-					9950	
	2732020			A1		1996		FR	1	.995-	1092	2		1.	9950	918
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	225417 1009625			B1 A3			0603		1	.995-	760			1	9950	01Ω
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	2108331			C1			0410			.995-:					9950	
	9501542			A			1215			995-					9950	
	691125			A5			0430			.995-				1	9950	918
	691431			A5			0731			000-					9950	
CH	691478			<b>A5</b>		2001	0731	CH	1	.995-2	2628			1	9950	918
	691594			A5		2001	0831	CH	1	.995-:	1780			1:	950	918
$\mathtt{PL}$	182450			В1		2002	0131	PL	1	.995-:	3105	18		1:	9950	918
	950483			B1			0228			.995-4					9950	
	187686			В1			0930			995-		17			9950	
	950482			B1		2007	0430	HR		.995-4					9950	
	502957			A1		2007	0615	AT		.995-:					9950	
WO	9609045	7) CT	7. T T	A1			0328			.995-1					9950	
								CA, C KP, K								
								PL, P								
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RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
                                            DE 1995-19534745
     DE 19534745
                          A1
                                19960404
                                                                    19950919
                          B4
                                20040609
     DE 19534745
                                19960409
                                            AU 1995-37186
                                                                    19950919
     AU 9537186
                          Α
                                            EE 1997-55
                                                                    19950919
                          В1
                                20010416
     EE 3386
                                            SK 1997-233
                                                                    19950919
     SK 283502
                          В6
                                20030805
                                            DE 1995-19549755
     DE 19549755
                          B4
                                20050504
                                                                    19950919
                                            DK 1997-27
                                19970109
                                                                    19970109
     DK 9700027
                          Α
     DK 175887
                          В1
                                20050523
                                19970109
                                            DK 1997-28
                                                                    19970109
     DK 9700028
                          Α
                          В1
                                20050523
     DK 175886
                                            CZ 2001-3548
                                                                    20011002
     CZ 290344
                          В6
                                20020717
                                            US 2002-83179
                                                                    20020226
     US 2002173645
                          A1.
                                20021121
                                            US 1994-308325
                                                                 A 19940919
PRIORITY APPLN. INFO.:
                                                                 A 19950426
                                            US 1995-427914
                                             US 1995-469093
                                                                 A1 19950606
                                             IL 1995-115315
                                                                 A3 19950914
                                            CZ 1995-2402
                                                                 A3 19950915
                                            DE 1995-19534744
                                                                 A1 19950919
                                            WO 1995-US11872
                                                                 W 19950919
```

Title compd. (I) (raloxifene hydrochloride) having a specified X-ray AB diffraction pattern, was prepared Thus, 6-methoxy-2-(4methoxyphenyl)benzo[b]thiophene (preparation given) and 4-(2piperidinoethoxy) benzoyl chloride hydrochloride (preparation given) in CH2Cl2 was treated with BCl3 at 0 for 8 h and at 35° for 16 h to give I.1,2dichloroethane of 86.8% purity. The latter in MeOH was treated with NaOH and activated C followed by filtration, treatment with HCl, and crystallization to give 99.1% pure I.

ANSWER 22 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN 1996:256453 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER:

124:289251

TITLE:

Process for preparing benzoic acid derivative

intermediates and benzothiophene pharmaceutical agents

INVENTOR(S):

Kjell, Douglas Patton; Perry, Fred Mason

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PAT	TENT NO.		KIND	DATE	APPLICATION NO.	DATE
		- <del>-</del> -				
ΕP	699672		. A1	19960306	EP 1995-306050	19950830
EP	699672		B1	19980422		
	R: AT,	BE,	CH, DE,	DK, ES, FR,	GB, GR, IE, IT, LI, I	LU, NL, PT, SE
US	5631369		A	19970520	US 1994-298636	19940831
ΙL	128881		Α	20001206	IL 1995-128881	19950828
CA	2157236		A1	19960301	CA 1995-2157236	19950830
FI	9504067		A	19960301	FI 1995-4067	19950830
HU	73141		A2	19960628	HU 1995-2537	19950830
HU	222121		B1	20030428		
BR	9503846		Α	19960917	BR 1995-3846	19950830
AΤ	165355		T	19980515	AT 1995-306050	19950830
ES	2114721		Т3	19980601	ES 1995-306050	19950830

TW 427975	В	20010401	TW	1995-84109069		19950830
JP 08119964	A·	19960514	JP	1995-223183		19950831
US 5750688	Α	19980512	US	1996-629862		19960409
PRIORITY APPLN. INFO.:			US	1994-298636	Α	19940831
			IL	1995-115092	A3	19950828

OTHER SOURCE(S):

MARPAT 124:289251

GI

AB The present invention provides a novel process for prepg. novel compds. of formula HO2C(p-C6H4)O(CH2)nNR1R2 [R1, R2 = C1-C4 alkyl, combine to form piperidinyl, pyrrolidinyl, methylpyrrolidinyl, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1-hexamethyleneimino; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2) nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compds. of formula RO2C(p-C6H4)OH [R = C1-C6 alkyl], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product of step (a) with an aqueous acid; and (c) cleaving the ester of the reaction product from step (b) to form an acid. The present invention further provides a novel process for preparing compds. of Formula I [R1, R2 = C1-C4 alkyl, or combine to form piperidinyl, pyrrolidino, methylpyrrolidino, dimethylpyrrolidinyl, morpholino, dimethylamino, diethylamino, or 1hexamethyleneimino; R3, R4 = H, hydroxy protecting group; n = 2, 3] or a pharmaceutically acceptable salt thereof, comprising (a) reacting a haloalkyl amine of formula X(CH2)nNR1R2 [X = halo; R1, R2, and n are as defined above], with a compound of formula RO2C(p-C6H4)OH [R = C1-C6 alky], in the presence of an alkyl acetate solvent and a base; (b) extracting the reaction product from step (a) with an aqueous acid; (c) cleaving the ester of the reaction product from step (b) to form an acid; (d) reacting the extracted product from step (c) with a compound of formula II [R3 and R4 are as defined above], or a pharmaceutically acceptable salt thereof; (e) optionally removing R3 and R4 hydroxy protecting groups of the reaction product from step (d); and (f) optionally forming a salt of the reaction from either steps (d) or step (e).

L6 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1996:150242 CAPLUS Full-text

DOCUMENT NUMBER:

124:202950

TITLE:

Preparation of benzothiophene glucopyranosides as

antihyperlipidemics.

INVENTOR(S):

Dodge, Jeffrey Alan; Frolik, Charles Alan; Lindstrom,

Terry Donald; Lugar, Charles Willis Iii; Staten,

Gilbert Stanley

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 20 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT NO.		KIND	DATE	AP	PLICATI	ON NO.		DATE
	683170		A1	1995112		1995-3	03265		19950516
EP	683170		B1	1999092					
•	R: AT,	BE, CH,	DE,	DK, ES, FR				LU, N	
US	5567820		Α	1996102	2 US	1995-4	04701		19950315
US	6723739		B1	2004042	) US	1995-4	05555		19950315
CA	2149501		A1	1995112	l CA	1995-2	149501		19950516
ZA	9503975		Α	1996111	B ZA	1995-3	975		19950516
AT	184880		T	1999101	5 AT	1995-3	03265		19950516
ES	2136799		Т3	1999120	l ES	1995-3	03265		19950516
AU	9520121		Α	1995113	UA C	1995-2	0121		19950517
AU	683734		B2	1997112	כ				
JР	07316180		A	1995120	5 JP	1995-1	18338		19950517
FI	9502420		Α	1995112	l FI	1995-2	420 .		19950518
NO	9501954		Α	1995112	l NO	1995-1	954		19950518
ио	304686		В1	1999020	L				
CN	1116626		Α	1996021	1 CN	1995-1	06322		19950518
CN	1039013		В	1998070	3				
BR	9502079		Α	1996030	5 BR	1995-2	079	•	19950518
HU	73788		A2	1996093	) HU	1995-1	466		19950518
HU	219335			2001032	3				
IL	113780		Α	1999062	) IL	1995-1	13780		19950518
GR	3032142		Т3	2000042	7 GR	1999-4	03228	i	19991215
	20041670	80	A1	2004082	us us	2004-7	78865		20040212
					US	1994-2	46655	A	19940520
							05555		19950315
ES AU AU JP FI NO CN CN BR HU HU IL GR	2136799 9520121 683734 07316180 9502420 9501954 304686 1116626 1039013 9502079 73788 219335 113780 3032142	80	T3 A B2 A A B1 A B1 A B1 A T3	1999120 1995113 1997112 1995120 1995112 1995112 1999020 1996021 1998070 1996030 1996093 2001032 1999062 2000042	L ES D AU D JP L FI L NO L CN B BR D HU B JI C GR G US US	1995-3 1995-2 1995-1 1995-1 1995-1 1995-1 1995-1 1995-1 1999-4 2004-7 1994-2	03265 0121 18338 420 954 06322 079 466 13780 03228 78865 46655	A	19950516 19950517 19950518 19950518 19950518 19950518 19950518 19950518 19950518 19950518 19950518 19991215 20040212 19940520

OTHER SOURCE(S):

CASREACT 124:202950

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II

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Raloxifene metabolites (I) and (II) and their hydrochloride salts were AB prepared Thus, I and II, prepared from 6-tert-butyldimethylsilylraloxifene and 4'-tert-butyldimethylsilylraloxifene and Me 1,2,3,4-0-tetraacetyl-Dglucopyranuronate, at 1.3 mg/kg in rats decreased serum cholesterol by 44.5% and 56.8%, resp. Drug formulations are given.

ANSWER 24 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN L6

1996:123714 CAPLUS Full-text ACCESSION NUMBER:

DOCUMENT NUMBER: 124:155994

Pharmaceutical compositions containing TITLE:

2-phenyl-3-aryoylbenzothiophenes for for inhibiting

bone loss and lowering serum cholesterol

Draper, Michael W. INVENTOR(S):

Eli Lilly and Co., USA PATENT ASSIGNEE(S): Can. Pat. Appl., 31 pp. SOURCE:

CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PAT	ENT	NO.			KINI	)	DATI	<b>Ξ</b>	2	ΑPI	PLICATION	NO.		:	DATE	
							-			-							
								199	50903			1995-214				19950	207
	US	5478	847					199	51226	τ	JS	1994-205	012			19940	302
	ZA	9500	976			A			50807		ZΑ	1995-976				19950	207
	NZ	3146	99			Α		2000	00728	1	ΙZ	1995-314	699			19950	207
	ΕP	6749	03			A1		199	51004	I	ΞP	1995-300	842			19950	210
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GI	R, IE, IT	, LI,	LU,	NL	, PT,	SE
	NO	9500	774			A		1999	50904	1	10	1995-774				19950	228
	RU	2100	024			C1		1997	71227	I	₹Ū	1995-102	778			19950	228
	RU	2150	275			C1		2000	00610	F	ขร	1996-119	781			19950	228
	AU	9513	551			A		1999	50907	7	U/	1995-135	51			19950	301
	AU	7025	75			B2		1999	90225								
	JP	0726	7861			Α		1999	51017	Ċ	JΡ	1995-417	69			19950	301
	JP	2818	384			B2		1998	31030								
	BR	9500	784			A			51024		3R	1995-784				19950	301
	CN	1119	530			Α		1996	50403	(	CN	1995-100	021			19950	301
	HU	7263	8			A2		1996	50528	ŀ	IJ	1995-634				19950	301
	JP	1029	1932			A		1998	31104	Ċ	JΡ	1998-107	550			19950	301
	JР	1031	0525			Α		1998	31124	Ċ	ΙP	1998-107	549			19950	301
	US	5610	168			A		1997	70311	٠ ر	JS	1995-422	289			19950	414
	US	5641	790			A		1997	70624	Ţ	JS	1995-422	417			19950	414
	US	5747	510			A		1998	30505	τ	JS	1997-788	984			19970	127
	US	3905				E1			50328		JS	2003-375	274		. :	20030	227
PRIOR	RITY	APP	LN.	INFO	. :					τ	JS	1994-205	012	I	<b>A</b>	19940	302
										Ċ	JΡ	1995-417	69	I	/3	19950	301
										τ	JS	1995-422	417	Į	11	19950	414
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A method of inhibiting bone loss or resorption, or lowering serum cholesterol, AB comprises administering to a human in need thereof pharmaceutical compns. containing 2-phenyl-3-aryoylbenzothiophenes, salt or solvate thereof, in a low dosage amount Raloxifene (I) at 50-200 mg decreased LDL cholesterol in postmenopausal women and there was no changes in HDL cholesterol level. A capsule contained I 150, starch 150, starch flowable powder 397, and silicone fluid 350 3.0 mg.

ANSWER 25 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1995:991025 CAPLUS Full-text

DOCUMENT NUMBER:

124:106673

TITLE:

Methods for lowering serum cholesterol

INVENTOR (S):

Black, Larry J.; Bryant, Henry U.; Cullinan, George

J.; Kauffman, Raymond F.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 14 pp. Cont.-in-part of U.S. Ser. No. 995, 222,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

GI

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5464845	Α	19951107	US 1993-159159	19931130
TW 383306	В	20000301	TW 1993-82100751	19930204
RU 2123335	C1	19981220	RU 1993-55026	19931213
ZA 9309427	A	19950615	ZA 1993-9427	19931215
SK 279271	B6	19980805	SK 1993-1421	19931215
IL 108042	Α	19980104	IL 1993-108042	19931216
CZ 283863	B6	19980617	CZ 1993-2790	19931216
HU 69686	A2	19950928	HU 1993-3676	19931220
HU 223342	B1	20040628		
RO 113806	B1	19981130	RO 1993-1739	19931220
PL 177349	B1	19991029	PL 1993-301579	19931220
CA 2112017	A1	19940623	CA 1993-2112017	19931221
CA 2112017	С	20050614		
NO 9304740	A	19940623	NO 1993-4740	19931221
	A	19940707	AU 1993-52578	19931221
AU 669235	B2	19960530		•
BR 9305182	A	19940816	BR 1993-5182	19931221
JP 06234632	Α	19940823	JP 1993-323825	19931222
JP 3197129	B2	20010813		
CN 1094042	Α	19941026	CN 1993-121277	19931222
CN 1043608	В	19990616	•	
AT 233559	T	20030315	AT 1993-310438	19931222
ES 2193142	Т3	20031101	ES 1993-310438	19931222
PRIORITY APPLN. INFO.:			US 1992-995222	B2 19921222
OTHER SOURCE(S):	MARPAT	124:106673		
a =			•	

AB A method of lowering serum cholesterol levels comprising administering to a patient a serum cholesterol lowering amount of a compound I wherein n is 0, 1 or 2; R is hydroxyl, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R1 is hydrogen, hydroxyl, chloro, bromo, methoxy, alkanoyloxy, cycloalkanoyloxy, substituted or unsubstituted aroyloxy, or substituted or unsubstituted aryloxycarbonyloxy; R2 is a heterocyclic ring (pyrrolidino, piperidino, or hexamethyleneimino); or a pharmaceutically acceptable salt or solvate thereof.

The tested compds. lowered LDL without significantly affecting primary sex targets.

L6 ANSWER 26 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:

1995:934099 CAPLUS Full-text

DOCUMENT NUMBER:

123:339764

TITLE:

Processes for preparing 3-(benzoyl)-2-(4-

hydroxyphenyl) benzothiophenes

INVENTOR(S):

Dodge, Jeffrey Alan; Stocksdale, Mark Gregory

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 19 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
EP 675121	A1	19951004	EP 1995-302076	19950328		
R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IE, IT, LI, LU,	NL, PT, SE		
CA 2145614	A1	19951001	CA 1995-2145614	19950327		
JP 07278138	A	19951024	JP 1995-73418	19950330		
US 5808061	Α	19980915	US 1995-503444	19950717		
PRIORITY APPLN. INFO.:			US 1994-220853	A 19940331		
OTHER SOURCE(S):	CASREA	CT·123:33976	4; MARPAT 123:339764			
GT						

The title compds. [I; R1R2 = C4-6 polymethylene, CH2CH(CH3)CH2CH2, CH2C(CH3)2CH2CH2, CH2CH2CH2CH2] [e.g., [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methan one hydrochloride], useful for the treatment of osteoporosis in post-menopausal women (no data), are prepared by: (a) coupling a benzothiophene (II; X = H) with a (hydroxyethyl)amine HOCH2CH2N(R1)R2 in the presence of P(Ph3) and di-Et azodicarboxylate; or (b) reacting a benzothiophene (II; X = CH2CH2Z; Z = leaving group) with pyrrolidine, piperidine, hexamethyleneimine, methylpyrrolidine, dimethylpyrrolidine, or morpholine; (c) deprotecting the 6-and 4-position hydroxy groups of the reaction product of step (a) or step (b);

and (d) optionally salifying or forming a solvate of the reaction product of step (c).

ANSWER 27 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1995:661193 CAPLUS Full-text

DOCUMENT NUMBER:

123:111843

TITLE:

2-amino-3-aroylbenzo[b] thiophenes and methods for

preparing and using same to produce 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2aminoethoxy) benzoyl] benzo [b] thiophene

INVENTOR(S): PATENT ASSIGNEE(S): Godfrey, Alexander G. Eli Lilly and Co., USA

SOURCE:

U.S., 9 pp.

DOCUMENT TYPE:

CODEN: USXXAM Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT 1	. 01			KIN	)	DATE		1	APPL	ICAT	ION I	NO.		D	ATE		
US	5420	349			Α		1995	0530	τ	JS 1	994-	25864	41		1	9940	610	
CA	21920	096			A1		1995	1221	(	CA 1	995-	2192	096		1	9950	607	
WO	9534	536			A1		1995	1221	7	VO 1	995-1	US73	99		1	9950	607	
	· W:	AM,																
		GB,	GE,	HU,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LK,	LR,	LT,	LU,	LV,	MD,	
		MG.	MN.	MW.	MX,	NO.	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	ΤJ,	
		TM,			•	•	•	•	•	•	•	•				•	-	
	RW:	KE,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,	
		LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML,	MR,	NE,	
•		SN,	TD,	TG														
AU	95282	236	•		Α		1996	0105	7	\U 1	995-	2823	6		1	9950	607	
EP	76415	50			<b>A1</b>		1997	0326	1	EP 1	995-	92380	04		1	9950	607	
	76415														•			
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	IT,	LI,	LU,	MC,	NL,	PT,	SE
HU.	76000	์ כ	-		A2		1997	0630	I	TU 1	996-	3404	•		1:	9950	607	
· HU	21383	34			В		1997	1028							•			
HU	76525	5			A2		1997	0929	I	łU 1	996-	3403			1:	9950	607	
HU	21627	72			В											•		
BR	95079	968			Α		1997	1118	I	3R 1	995-	7968			1	9950	607	
JP	10503	3175			T						996-							
	18605				T		1999	1115	7	AT 1	995-	92380	04		. 1:	9950	607	
ES	21392	222			Т3		2000	0201	I	ES 1	995-	92380	04		1:	9950	607	
HU	21782	22									998-							
FI	96048	354			Α		1996	1204	1	7I 1	996-	4854			1	9961	204	
GR	30324	109					2000	0531	(	3R 2	000-4	40010	06					
PRIORIT											994-							
									V	VO 1	995-1	US739	9 9	Ţ	W 1	9950	507	
OTHER SO	OURCE	(s):			CASI	REAC	T 12	3:11	1843	MA	RPAT	123	: 111	843				

GΙ

A group of 2-amino-3-aroyl-benzo[b]thiophenes (I) are prepd. by prepg. an  $\alpha$ -AB hydroxy thioacetamide 4-ROC6H4CH(OH)C(:S)NR9R9 (II) wherein R, R8 and R9 independently represent C1-C6 alkyl; comprising: (a) reacting an alkyl imidate of the formula 4-ROC6H4CH(OH)C(:NH.protic acid)OR''' where R''' is C1-C6 alkyl, with a sulfur compound to yield a thioester of the formula 4-ROC6H4CH(OH)C(:S)OR'''; (b) reacting the thioester with a dialkylamine of the formula HNR8R9 to yield the  $\alpha$ -hydroxy thioacetamide; said steps being conducted without isolation or purification of the thioester., cyclizing II, and subsequently acylating the benzo[b]thiophene to yield the 2-amino-3-aryl derivative These compds. may be treated with suitable Ph Grignard reagents, and after deprotection, yield 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2piperidinoethoxy)benzoyl]benzo[b]thi ophene. %Thus, e.g., p-anisaldehyde was converted to p- methoxybenzaldehyde cyanohydrin (80% yield) and subsequently to the Me imidate 4-MeOC6H4CH(OH)C(:NH.HCl)OMe (85-90% yield); reaction of the latter with H2S/Me2NH afforded  $\alpha$ -(4-methoxy phenyl)- $\alpha$ -hydroxy- N,Ndimethylthioacetamide (70%) which was cyclized with methanesulfonic acid to 2-N, N-dimethylamino-6-methoxybenzo[b] thiophene (79%); acylation of the latter with 4-(2-piperidinoethoxy) benzoyl chloride hydrochloride (autocatalytic) afforded 2-N, N-dimethylamino-6-methoxy-3-[4-(2piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (I; R = Me, R3 = R4 = Me, R'' = 2-piperidinoethyl; 74%) which underwent Grignard reaction with 4methoxyphenylmagnesium bromide to afford 2-(4-methoxyphenyl)-6- methoxy-3-[4-(piperidinoethoxy)benzoyl]benzo[b]thiophene hydrochloride (90%); deprotection of the latter with AlCl3/propanethiol afforded 6-hydroxy-2-(4-hydroxyphenyl)-3-[4-(2-piperidinoethoxy)benzoyl]benzo[b]thi ophene hydrochloride (95% yield).

ANSWER 28 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN. ACCESSION NUMBER: 1995:362913 CAPLUS Full-text

Т

DOCUMENT NUMBER:

122:213884

TITLE:

A chemical probe for the estrogen receptor: synthesis

of the 3H-isotopomer of raloxifene

AUTHOR(S):

Dodge, Jeffrey A.; Stocksdale, Mark G.; Jones, C.

David

CORPORATE SOURCE:

Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

SOURCE:

Journal of Labelled Compounds & Radiopharmaceuticals

(1995), 36(1), 43-9

CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER:

Wiley

DOCUMENT TYPE: Journal LANGUAGE: English

Radiolabeled raloxifene (LY156758) was prepd. by tritium gas hydrogenolysis of AB a 3-aroyl bis-brominated precursor. The requisite halogenated intermediate was accessed by regioselective aroylation of 6-methoxy-2-(4methoxyphenyl)benzo[b]thiophene with 3,5-dibromo-4-[2-(1piperdinyl)ethoxy]benzoyl chloride. Selective deprotection of the aryl Me ethers in the presence of the ethoxy side-chain followed by palladium

catalyzed halogen-tritum exchange provided the target compound with a specific activity of 30.1 Ci/mmol.

L6 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1987:433189 CAPLUS Full-text

DOCUMENT NUMBER: 107:33189

TITLE: Treatment of mammary cancer

INVENTOR(S): Black, Larry J.; Clemens, James A.

PATENT ASSIGNEE(S): Eli Lilly and Co., USA

SOURCE: U.S., 10 pp. Cont. of U.S. Ser. No. 289,360,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PRIO	US 4656187	A	19870407	US 1983-556875 US 1981-289360	19831201
מא	A mothod of inhibit	ina th	arouth of	estrogen-dependent m	
AB	comprises administed hydroxyphenyl) -3-[4.apprx.5 mg/kg/day combination comprised weight of II. I hypyrrolidinoethoxy) 2-(4-methoxyphenyl)	ering all 1-(2-py) of a 2 ses .appydrochlo penzoic benzo[l	cout 20 mg/k rrolidinoeth nd compound orx.4 parts oride was pr acid with to olthiophene	g/day of a 1st composition of a 1st composition of I and by weight of I and hionyl chloride and	ound 6-hydroxy-2-(4- th iophene (I) and so, a pharmaceutical apprx.1 part by 4-(2- then with 6-methoxy- choxybenzenethiol and
	given for 8 wks to receiving the combitumors. The rest 1	rats wination had only	ith induced treatment e y a very mod	mammary tumors. Hall experienced a total rest growth of their	lf of the rats regression of their
	treatment. A syne	GISCIC	errect was	SHOWII.	

L6 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1984:448784 CAPLUS Full-text

DOCUMENT NUMBER: 101:48784

TITLE: Antiestrogens. 2. Structure-activity studies in a

series of 3-aroyl-2-arylbenzo[b]thiophene derivatives leading to [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone

hydrochloride (LY 156758), a remarkably effective estrogen antagonist with only minimal intrinsic

estrogenicity

AUTHOR(S): Jones, Charles D.; Jevnikar, Mary G.; Pike, Andrew J.;

Peters, Mary K.; Black, Larry J.; Thompson, Allen R.;

Falcone, Julie F.; Clemens, James A.

CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN,

46285, USA

SOURCE: Journal of Medicinal Chemistry (1984), 27(8), 1057-66

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

In an effort to prep. nonsteroidal antiestrogens demonstrating greater AB antagonism and less intrinsic estrogenicity than those currently available, a series of 3-aroyl-2-arylbenzo[b]thiophene derivs. was synthesized. These compds. were prepared by Friedel-Crafts aroylation of appropriate O-protected 2-arylbenzo[b]thiophene nuclei with basic side-chain-bearing benzoyl chlorides followed by removal of the protective groups to provide the desired compds. containing both hydroxyl and basic side-chain functionality. A particularly useful method for the cleavage of aryl methoxy ethers without removal of (dialkylamino)ethoxy side chain functionality elsewhere in the mol. was The benzothiophene derivs. were tested for their ability to AlCl3/EtSH. inhibit the growth-stimulating action of estradiol on the immature rat uterus. Seemingly minor changes in the side-chain amine moiety had profound effects on the ability of the compds. to antagonize estradiol. Analogs having basic side chains containing cyclic (pyrrolidine, piperidine, and hexamethyleneamine) moieties had less intrinsic estrogenicity and antagonized estradiol action more completely than their noncyclic counterparts. The most effective antiestrogen in the series, [6-hydroxy-2-(4-hydroxyphenyl)benzo[b]thien-3-yl]-[4-[2-(1- piperidinyl)ethoxy]phenyl]methanone (I) [84449-90-1], elicited a modest uterotropic activity that did not increase with increasing dose. In antagonism of estradiol, I exhibited a degree of inhibition surpassing that of tamoxifen at any dose tested. The new benzothiophene antiestrogen also had high affinity for rat uterine cytoplasmic estrogen receptor and was an inhibitor of the growth of DMBA-induced rat mammary tumors.

L6 ANSWER 31 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER: 1984:156501 CAPLUS Full-text

DOCUMENT NUMBER:

100:156501

TITLE:

Antiestrogenic and antiandrogenic benzothiophenes

INVENTOR(S):

Jones, Charles D.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 23 pp. Cont.-in-part of U.S. Ser. No. 246,335,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	AP	PLICATION NO.		DATE
US 4418068	· <b>A</b>	19831129	US	1981-331042		19811216
ZA 8202247	Α	19831130	ZA	1982-2247		19820401
PRIORITY APPLN. INFO.:			US	1981-246335	A2	19810403
OTHER SOURCE(S):	CASRE	ACT 100:1565	01			
GI	•				•	

Antiandrogenic and antiestrogenic [(piperidinoethoxy)benzoyl]benzothiophen es AB I [R,R1 = H, R2CO; R2 = H, cycloalkyl, (un) substituted alkyl, Ph] were prepared Thus, 2-(4-hydroxyphenyl)benzo[b]thiophene-6-ol was esterified with MeSO2Cl and the diester subjected to Friedel-Crafts acylation with 4-(2piperidinoethoxy) benzoyl chloride to give I (R = R1 = MeSO2). This was saponified to give I (R = R1 = H) (II). Immature female rats administered  $0.03~\mu g$  estradiol propionate (III) s.c. together with 3 mg II s.c. daily for 4 d had average uterus weight of 21.3 mg. Those given III alone had average uterus weight of 65.9 mg. I also were effective as antiandrogens and as mammary tumor inhibitors.

Ι

CAPLUS COPYRIGHT 2007 ACS on STN 1.6 ANSWER 32 OF 34

ACCESSION NUMBER:

1983:422309 CAPLUS Full-text

DOCUMENT NUMBER:

99:22309

TITLE:

Acylated benzothiophenes

INVENTOR(S):

Peters, Mary K.

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 246,333,

abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4380635	Α	19830419	US 1981-331046	
CA 1167036	<b>A</b> 1	19840508	CA 1982-400262	19820331
EP 62505	A1	19821013	EP 1982-301739	19820401
EP 62505	B1	19850724		
R: AT, BE, CH,	DE, FR	, GB, IT,	LU, NL, SE	•
GB 2096608	A	19821020	GB 1982-9681	19820401
GB 2096608	В	19850612		
DD 201794	A5	19830810	DD 1982-238653	19820401
CS 227347	B2	19840416	CS 1982-2356	19820401
RO 84584	A1	19840717	RO 1982-107118	19820401
PL 130584	B1	19840831	PL 1982-235751	19820401
AT 14429	T	19850815	AT 1982-301739	19820401
DK 8201513	A	19821004	DK 1982-1513	19820402
FI 8201161	A	19821004	FI 1982-1161	19820402
JP 57181079	$\cdot \mathbf{A}$	19821108	JP 1982-56481	19820402
ES 511123	<b>A1</b>	19830216	ES 1982-511123	19820402
HU 28746	A2	19831228	HU 1982-1025	19820402
HU 191084	B .	19870128		
SU 1138028	<b>A3</b>	19850130	SU 1982-3417251	19820402
PRIORITY APPLN. INFO.:			US 1981-246333	A2 19810403
			US 1981-246335	A 19810403

The acylated benzothiophenones I (R,R1 = C1-4 alkyl, RR1 = polymethylene, AΒ CH2CHMeCH2CH2, CH2CH2OCH2CH2) were prepared by acylation-demethylation of benzothiophenes II. Thus, 3-MeOC6H4SN was treated with BrCH2COC6H4OMe-p followed by cyclization to give II, which was treated with AlCl3 and the acid chloride of 4-(2-piperidinoethoxy) benzoic acid to give I (NRR1 = piperidino).

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN ACCESSION NUMBER:

1983:71918 CAPLUS Full-text

DOCUMENT NUMBER:

98:71918

TITLE:

Acylated benzothiophenes

INVENTOR(S):

Peters, Mary Kathleen; Jones, Charles David

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA

SOURCE:

Eur. Pat. Appl., 29 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
	`			-	
· EP 62505	A1	19821013	EP 1982-301739		19820401
EP 62505	B1	19850724			
R: AT, BE, CH,	DE, FR	, GB, IT,	LU, NL, SE		
US 4380635	A	19830419	US 1981-331046		19811216
AT 14429	T	19850815	AT 1982-301739		19820401
PRIORITY APPLN. INFO.:			US 1981-246333	Α	19810403
			US 1981-246335	Α	19810403
			US 1981-331045	Α	19811216
			US 1981-331046	Α	19811216
	•	•	EP 1982-301739	Α	19820401
OTHER SOURCE(S):	MARPAT	98:71918			

GΙ

3-[4-(2-Aminoethoxy)benzoyl]benzothiophenes I [R, R1 = C1-4 alkyl; RR1 = AB (CH2)4, (CH2)5, (CH2)6, CH2CHMeCH2CH2, CH2CH2OCH2CH2], useful as antiestrogens (no data), were prepared by acylating benzothiophene II. Thus, heating 3-MeOC6H4SCH2COC6H4OMe-4 with polyphosphoric acid gave II, which was acylated by 4-(Me2NCH2CH2O)C6H4CO2H.HCl and SOCl2 in PhCl-CH2Cl2 containing DMF and AlCl3 to give I (R = R1 = Me).

ANSWER 34 OF 34 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:

1983:71917 CAPLUS Full-text

DOCUMENT NUMBER:

98:71917

TITLE:

Benzothiophene compounds

INVENTOR (S):

Jones, Charles David

PATENT ASSIGNEE(S):

Eli Lilly and Co., USA Eur. Pat. Appl., 107 pp.

SOURCE:

CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 62503	A1	19821013	EP 1982-301737	19820401
R: BE, CH, DE,	FR, GB	, IT, LU, NI	C, SE	
AU 8282265	A	19821007	AU 1982-82265	19820401
AU 555658	B2	19861002		
GB 2097788	A	19821110	GB 1982-9680	19820401
GB 2097788	В	19850424		
JP 57181081	Α.	19821108	JP 1982-56479	19820402
PRIORITY APPLN. INFO.:			US 1981-246335 A	19810403
			US 1981-331045 A	19811216

GI

$$CO$$
 $OCH_2CH_2N$ 
 $Z$ 
 $OCH_2CH_2R$ 
 AB [(Aminoethoxy)benzoyl]benzothiophenes I (Z = CH2CH2CH2, CHMeCH2) were prepared, and limited the increase of uterine weight in rats treated with estradiol. Thus, treating II (R = Br) with 3-methylpyrrolidine in DMF containing KI gave II (R = 3-methyl-1-pyrrolidinyl) which was deprotected by NaOH to give I (Z = CHMeCH2).